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(54) Title: COMPOSITIONS, SPLICE VARIANTS AND METHODS RELATING TO COLON SPECIFIC GENES AND PROTEINS

(57) Abstract: The present invention relates to newly identified nucleic acid molecules and polypeptides present in normal and neoplastic colon cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions containing the nucleic acid molecules, polypeptides, antibodies, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating colon cancer and non-cancerous disease states in colon, identifying colon tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered colon tissue for treatment and research.

WO 2004/050858 A2

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COMPOSITIONS, SPLICE VARIANTS AND METHODS RELATING TO COLON SPECIFIC GENES AND PROTEINS

5

INTRODUCTION

This application claims the benefit of priority from U.S. Provisional Patent Application Serial No. 60/431,133 filed December 4, 2002, which is herein incorporated by reference in its entirety.

FIELD OF THE INVENTION

10 The present invention relates to newly identified nucleic acids and polypeptides present in normal and neoplastic colon cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions comprising the nucleic acids,
15 polypeptides, antibodies, post translational modifications (PTMs), variants, derivatives, agonists and antagonists thereof and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating colon cancer and/or non-cancerous disease states in colon, identifying colon tissue and monitoring and identifying and/or designing agonists and antagonists of polypeptides of
20 the invention. The uses also include gene therapy, therapeutic molecules including but not limited to antibodies or antisense molecules, production of transgenic animals and cells, and production of engineered colon tissue for treatment and research.

BACKGROUND OF THE INVENTION

Colorectal cancer is the second most common cause of cancer death in the United
25 States and the third most prevalent cancer in both men and women. M. L. Davila & A. D. Davila, *Screening for Colon and Rectal Cancer*, in Colon and Rectal Cancer 47 (Peter S. Edelstein ed., 2000). The American Cancer Society estimates that there will be about 105,500 new cases of colon cancer and 42,000 new cases of rectal cancer in 2003 in the United States. Colon cancer and rectal cancer will cause about 57,100 deaths combined.
30 ACS Website: cancer.org on the world wide web. Nearly all cases of colorectal cancer arise from adenomatous polyps, some of which mature into large polyps, undergo abnormal growth and development, and ultimately progress into cancer. Davila at 55-56. This progression would appear to take at least 10 years in most patients, rendering it a

readily treatable form of cancer if diagnosed early, when the cancer is localized. Davila at 56; Walter J. Burdette, Cancer: Etiology, Diagnosis, and Treatment 125 (1998).

Although our understanding of the etiology of colon cancer is undergoing continual refinement, extensive research in this area points to a combination of factors, including age, hereditary and nonhereditary conditions, and environmental/dietary factors. Age is a key risk factor in the development of colorectal cancer, Davila at 48, with men and women over 40 years of age becoming increasingly susceptible to that cancer, Burdette at 126. Incidence rates increase considerably in each subsequent decade of life. Davila at 48. A number of hereditary and nonhereditary conditions have also been linked to a heightened risk of developing colorectal cancer, including familial adenomatous polyposis (FAP), hereditary nonpolyposis colorectal cancer (Lynch syndrome or HNPCC), a personal and/or family history of colorectal cancer or adenomatous polyps, inflammatory bowel disease, diabetes mellitus, and obesity. Davila at 47; Henry T. Lynch & Jane F. Lynch, *Hereditary Nonpolyposis Colorectal Cancer (Lynch Syndromes)*, in Colon and Rectal Cancer 67-68 (Peter S. Edelstein ed., 2000).

Environmental/dietary factors associated with an increased risk of colorectal cancer include a high fat diet, intake of high dietary red meat, and sedentary lifestyle. Davila at 47; Reddy, B. S., *Prev. Med.* 16(4): 460-7 (1987). Conversely, environmental/dietary factors associated with a reduced risk of colorectal cancer include a diet high in fiber, folic acid, calcium, and hormone-replacement therapy in post-menopausal women. Davila at 50-55. The effect of antioxidants in reducing the risk of colon cancer is unclear. Davila at 53.

Because colon cancer is highly treatable when detected at an early, localized stage, screening should be a part of routine care for all adults starting at age 50, especially those with first-degree relatives with colorectal cancer. One major advantage of colorectal cancer screening over its counterparts in other types of cancer is its ability to not only detect precancerous lesions, but to remove them as well. Davila at 56. The key colorectal cancer screening tests in use today are fecal occult blood test, sigmoidoscopy, colonoscopy, double-contrast barium enema, and the carcinoembryonic antigen (CEA) test. Burdette at 125; Davila at 56.

The fecal occult blood test (FOBT) screens for colorectal cancer by detecting the amount of blood in the stool, the premise being that neoplastic tissue, particularly malignant tissue, bleeds more than typical mucosa, with the amount of bleeding increasing

with polyp size and cancer stage. Davila at 56-57. While effective at detecting early stage tumors, FOBT is unable to detect adenomatous polyps (premalignant lesions), and, depending on the contents of the fecal sample, is subject to rendering false positives.

Davila at 56-59. Sigmoidoscopy and colonoscopy, by contrast, allow direct visualization
5 of the bowel, and enable one to detect, biopsy, and remove adenomatous polyps. Davila at 59-60, 61. Despite the advantages of these procedures, there are accompanying downsides: sigmoidoscopy, by definition, is limited to the sigmoid colon and below, colonoscopy is a relatively expensive procedure, and both share the risk of possible bowel perforation and hemorrhaging. Davila at 59-60. Double-contrast barium enema (DCBE)
10 enables detection of lesions better than FOBT, and almost as well a colonoscopy, but it may be limited in evaluating the winding rectosigmoid region. Davila at 60. The CEA blood test, which involves screening the blood for carcinoembryonic antigen, shares the downside of FOBT, in that it is of limited utility in detecting colorectal cancer at an early stage. Burdette at 125.

15 Once colon cancer has been diagnosed, treatment decisions are typically made in reference to the stage of cancer progression. A number of techniques are employed to stage the cancer (some of which are also used to screen for colon cancer), including pathologic examination of resected colon, sigmoidoscopy, colonoscopy, and various imaging techniques. AJCC Cancer Staging Handbook 84 (Irvin D. Fleming et al. eds., 5th
20 ed. 1998); Montgomery, R. C. and Ridge, J.A., *Semin. Surg. Oncol.* 15(3): 143-150 (1998). Moreover, chest films, liver functionality tests, and liver scans are employed to determine the extent of metastasis. Fleming at 84. While computerized tomography and magnetic resonance imaging are useful in staging colorectal cancer in its later stages, both have unacceptably low staging accuracy for identifying early stages of the disease, due to
25 the difficulty that both methods have in (1) revealing the depth of bowel wall tumor infiltration and (2) diagnosing malignant adenopathy. Thoeni, R. F., *Radiol. Clin. N. Am.* 35(2): 457-85 (1997). Rather, techniques such as transrectal ultrasound (TRUS) are preferred in this context, although this technique is inaccurate with respect to detecting small lymph nodes that may contain metastases. David Blumberg & Frank G. Opelka,
30 *Neoadjuvant and Adjuvant Therapy for Adenocarcinoma of the Rectum*, in Colon and Rectal Cancer 316 (Peter S. Edelstein ed., 2000).

Several classification systems have been devised to stage the extent of colorectal cancer, including the Dukes' system and the more detailed International Union against

Cancer-American Joint Committee on Cancer TNM staging system, which is considered by many in the field to be a more useful staging system. Burdette at 126-27. The TNM system, which is used for either clinical or pathological staging, is divided into four stages, each of which evaluates the extent of cancer growth with respect to primary tumor (T),
5 regional lymph nodes (N), and distant metastasis (M). Fleming at 84-85. The system focuses on the extent of tumor invasion into the intestinal wall, invasion of adjacent structures, the number of regional lymph nodes that have been affected, and whether distant metastasis has occurred. Fleming at 81.

Stage 0 is characterized by *in situ* carcinoma (Tis), in which the cancer cells are
10 located inside the glandular basement membrane (intraepithelial) or lamina propria (intramucosal). In this stage, the cancer has not spread to the regional lymph nodes (N0), and there is no distant metastasis (M0). In stage I, there is still no spread of the cancer to the regional lymph nodes and no distant metastasis, but the tumor has invaded the submucosa (T1) or has progressed further to invade the muscularis propria (T2). Stage II
15 also involves no spread of the cancer to the regional lymph nodes and no distant metastasis, but the tumor has invaded the subserosa, or the nonperitonealized pericolic or perirectal tissues (T3), or has progressed to invade other organs or structures, and/or has perforated the visceral peritoneum (T4). Stage III is characterized by any of the T substages, no distant metastasis, and either metastasis in 1 to 3 regional lymph nodes (N1)
20 or metastasis in four or more regional lymph nodes (N2). Lastly, stage IV involves any of the T or N substages, as well as distant metastasis. Fleming at 84-85; Burdette at 127.

Currently, pathological staging of colon cancer is preferable over clinical staging as pathological staging provides a more accurate prognosis. Pathological staging typically involves examination of the resected colon section, along with surgical examination of the
25 abdominal cavity. Fleming at 84. Clinical staging would be a preferred method of staging were it at least as accurate as pathological staging, as it does not depend on the invasive procedures of its counterpart.

Turning to the treatment of colorectal cancer, surgical resection results in a cure for roughly 50% of patients. Irradiation is used both preoperatively and postoperatively in
30 treating colorectal cancer. Chemotherapeutic agents, particularly 5-fluorouracil, are also powerful weapons in treating colorectal cancer. Other agents include irinotecan and floxuridine, cisplatin, levamisole, methotrexate, interferon- α , and leucovorin. Burdette at 125, 132-33. Nonetheless, thirty to forty percent of patients will develop a recurrence of

colon cancer following surgical resection, which in many patients is the ultimate cause of death. Wayne De Vos, *Follow-up After Treatment of Colon Cancer, Colon and Rectal Cancer* 225 (Peter S. Edelstein ed., 2000). Accordingly, colon cancer patients must be closely monitored to determine response to therapy and to detect persistent or recurrent disease and metastasis.

The next few paragraphs describe the some of molecular bases of colon cancer. In the case of FAP, the tumor suppressor gene APC (adenomatous polyposis coli), chromosomally located at 5q21, has been either inactivated or deleted by mutation. Alberts et al., *Molecular Biology of the Cell* 1288 (3d ed. 1994). The APC protein plays a role in a number of functions, including cell adhesion, apoptosis, and repression of the *c-myc* oncogene. N. R. Hall & R. D. Madoff, *Genetics and the Polyp-Cancer Sequence, Colon and Rectal Cancer* 8 (Peter S. Edelstein, ed., 2000). Of those patients with colorectal cancer who have normal APC genes, over 65% have such mutations in the cancer cells but not in other tissues. Alberts et al., *supra* at 1288. In the case of HNPCC, patients manifest abnormalities in the tumor suppressor gene HNPCC, but only about 15% of tumors contain the mutated gene. *Id.* A host of other genes have also been implicated in colorectal cancer, including the *K-ras*, *N-ras*, *H-ras* and *c-myc* oncogenes, and the tumor suppressor genes *DCC* (deleted in colon carcinoma) and *p53*. Hall & Madoff, at 8-9; Alberts et al., at 1288.

Abnormalities in Wg/Wnt signal transduction pathway are also associated with the development of colorectal carcinoma. Taipale, J. and Beachy, P.A. *Nature* 411: 349-354 (2001). Wnt1 is a secreted protein gene originally identified within mouse mammary cancers by its insertion into the mouse mammary tumor virus (MMTV) gene. The protein is homologous to the wingless (Wg) gene product of *Drosophila*, in which it functions as an important factor for the determination of dorsal-ventral segmentation and regulates the formation of fly imaginal discs. Wg/Wnt pathway controls cell proliferation, death and differentiation. Taipal (2001). There are at least 13 members in the Wnt family. These proteins have been found expressed mainly in the central nervous system (CNS) of vertebrates as well as other tissues such as mammary and intestine. The Wnt proteins are the ligands for a family of seven transmembrane domain receptors related to the Frizzled gene product in *Drosophila*. Binding Wnt to Frizzled stimulates the activity of the downstream target, Dishevelled, which in turn inactivates the glycogen synthase kinase β (GSK3 β). Taipal (2001). Usually active GSK3 β will form a complex with the

adenomatous polyposis coli (APC) protein and phosphorylate another complex member, β -catenin. Once phosphorylated, β -catenin is directed to degradation through the ubiquitin pathway. When GSK3 β or APC activity is down regulated, β -catenin is accumulated in the cytoplasm and binds to the T-cell factor or lymphocyte excitation factor (Tcf/Lef) family of transcriptional factors. Binding of β -catenin to Tcf releases the transcriptional repression and induces gene transcription. Among the genes regulated by β -catenin are a transcriptional repressor Engrailed, a transforming growth factor- β (TGF- β) family member Decapentaplegic, and the cytokine Hedgehog in *Drosophila*. β -Catenin is also involved in regulating cell adhesion by binding to α -catenin and E-cadherin. On the other hand, binding of β -catenin to these proteins controls the cytoplasmic β -catenin level and its complexing with TCF. Taipal (2001). Growth factor stimulation and activation of c-src or v-src also regulate β -catenin level by phosphorylation of α -catenin and its related protein, p120^{cas}. When phosphorylated, these proteins decrease their binding to E-cadherin and β -catenin resulting in the accumulation of cytoplasmic β -catenin. Reynolds, A.B. et al. *Mol. Cell Biol.* 14: 8333-8342 (1994). In colon cancer, c-src enzymatic activity has been shown to be increased to the level of v-src. Alternation of components in the Wg/Wnt pathway promotes colorectal carcinoma development. The best known modifications are to the APC gene. Nicola S et al. *Hum. Mol. Genet* 10:721-733 (2001). This germline mutation causes the appearance of hundreds to thousands of adenomatous polyps in the large bowel. It is the gene defect that accounts for the autosomally dominantly inherited FAP and related syndromes. The molecular alternations that occur in this pathway largely involve deletions of alleles of tumor-suppressor genes, such as APC, p53 and Deleted in Colorectal Cancer (DCC), combined with mutational activation of proto-oncogenes, especially c-Ki-ras. Aoki, T. et al. *Human Mutat.* 3: 342-346 (1994). All of these lead to genomic instability in colorectal cancers.

Another source of genomic instability in colorectal cancer is the defect of DNA mismatch repair (MMR) genes. Human homologues of the bacterial *mutHLS* complex (hMSH2, hMLH1, hPMS1, hPMS2 and hMSH6), which is involved in the DNA mismatch repair in bacteria, have been shown to cause the HNPCC (about 70-90% HNPCC) when mutated. Modrich, P. and Lahue, R. *Ann Rev. Biochem.* 65: 101-133 (1996); and Peltomäki, P. *Hum. Mol. Genet* 10: 735-740 (2001). The inactivation of these proteins leads to the accumulation of mutations and causes genetic instability that represents errors

in the accurate replication of the repetitive mono-, di-, tri- and tetra-nucleotide repeats, which are scattered throughout the genome (microsatellite regions). Jass, J.R. et al. *J. Gastroenterol Hepatol* 17: 17-26 (2002). Like in the classic FAP, mutational activation of c-Ki-ras is also required for the promotion of MSI in the alternative HNPCC. Mutations
5 in other proteins such as the tumor suppressor protein phosphatase PTEN (Zhou, X.P. et al. *Hum. Mol. Genet* 11: 445-450 (2002)), BAX (Buttler, L.M. *Aus. N. Z. J. Surg.* 69: 88-94 (1999)), Caspase-5 (Planck, M. *Cancer Genet Cytogenet.* 134: 46-54 (2002)), TGF β -RII (Fallik, D. et al. *Gastroenterol Clin Biol.* 24: 917-22 (2000)) and IGFII-R (Giovannucci E. *J. Nutr.* 131: 3109S-20S (2001)) have also been found in some colorectal
10 tumors possibly as the cause of MMR defect.

Some tyrosine kinases have been shown up-regulated in colorectal tumor tissues or cell lines like HT29. Skoudy, A. et al. *Biochem J.* 317 (Pt 1): 279-84 (1996). Focal adhesion kinase (FAK) and its up-stream kinase c-src and c-yes in colonic epithelial cells may play an important role in the promotion of colorectal cancers through the extracellular
15 matrix (ECM) and integrin-mediated signaling pathways. Jessup, J.M. et al., *The molecular biology of colorectal carcinoma*, in: The Molecular Basis of Human Cancer, 251-268 (Coleman W.B. and Tsongalis G.J. Eds. 2002). The formation of c-src/FAK complexes may coordinately deregulate VEGF expression and apoptosis inhibition. Recent evidences suggest that a specific signal-transduction pathway for cell survival that
20 implicates integrin engagement leads to FAK activation and thus activates PI-3 kinase and akt. In turn, akt phosphorylates BAD and blocks apoptosis in epithelial cells. The activation of c-src in colon cancer may induce VEGF expression through the hypoxia pathway. Other genes that may be implicated in colorectal cancer include Cox enzymes (Ota, S. et al. *Aliment Pharmacol. Ther.* 16 (Suppl 2): 102-106 (2002)), estrogen (al-
25 Azzawi, F. and Wahab, M. *Climacteric* 5: 3-14 (2002)), peroxisome proliferator-activated receptor- γ (PPAR- γ) (Gelman, L. et al. *Cell Mol. Life Sci.* 55: 932-943 (1999)), IGF-I (Giovannucci (2001)), thymine DNA glycosylase (TDG) (Hardeland, U. et al. *Prog. Nucleic Acid Res. Mol. Biol.* 68: 235-253 (2001)) and EGF (Mendelsohn, J. *Endocrine-Related Cancer* 8: 3-9 (2001)).

30 Gene deletion and mutation are not the only causes for development of colorectal cancers. Epigenetic silencing by DNA methylation also accounts for the loss of function of colorectal cancer suppressor genes. A strong association between MSI and CpG island methylation has been well characterized in sporadic colorectal cancers with high MSI but

not in those of hereditary origin. In one experiment, DNA methylation of MLH1, CDKN2A, MGMT, THBS1, RARB, APC, and p14ARF genes has been shown in 80%, 55%, 23%, 23%, 58%, 35%, and 50% of 40 sporadic colorectal cancers with high MSI respectively. Yamamoto, H. et al. *Genes Chromosomes Cancer* 33: 322-325 (2002); and
5 Kim, K.M. et al. *Oncogene*. 12;21(35): 5441-9 (2002). Carcinogen metabolism enzymes such as GST, NAT, CYP and MTHFR are also associated with an increased or decreased colorectal cancer risk. Pistorius, S. et al. *Kongressbd Dtsch Ges Chir Kongr* 118: 820-824 (2001); and Potter, J.D. *J. Natl. Cancer Inst.* 91: 916-932 (1999).

From the foregoing, it is clear that procedures used for detecting, diagnosing,
10 monitoring, staging, prognosticating, and preventing the recurrence of colorectal cancer are of critical importance to the outcome of the patient. Moreover, current procedures, while helpful in each of these analyses, are limited by their specificity, sensitivity, invasiveness, and/or their cost. As such, highly specific and sensitive procedures that would operate by way of detecting novel markers in cells, tissues, or bodily fluids, with
15 minimal invasiveness and at a reasonable cost, would be highly desirable.

Accordingly, there is a great need for more sensitive and accurate methods for predicting whether a person is likely to develop colorectal cancer, for diagnosing colorectal cancer, for monitoring the progression of the disease, for staging the colorectal cancer, for determining whether the colorectal cancer has metastasized, and for imaging
20 the colorectal cancer. Following accurate diagnosis, there is also a need for less invasive and more effective treatment of colorectal cancer.

Growth and metastasis of solid tumors are also dependent on angiogenesis. Folkman, J., 1986, *Cancer Research*, 46, 467-473; Folkman, J., 1989, *Journal of the National Cancer Institute*, 82, 4-6. It has been shown, for example, that tumors which
25 enlarge to greater than 2 mm must obtain their own blood supply and do so by inducing the growth of new capillary blood vessels. Once these new blood vessels become embedded in the tumor, they provide a means for tumor cells to enter the circulation and metastasize to distant sites such as liver, lung or bone. Weidner, N., et al., 1991, *The New England Journal of Medicine*, 324(1), 1-8.

30 Angiogenesis, defined as the growth or sprouting of new blood vessels from existing vessels, is a complex process that primarily occurs during embryonic development. The process is distinct from vasculogenesis, in that the new endothelial cells lining the vessel arise from proliferation of existing cells, rather than differentiating from

stem cells. The process is invasive and dependent upon proteolysis of the extracellular matrix (ECM), migration of new endothelial cells, and synthesis of new matrix components. Angiogenesis occurs during embryonic development of the circulatory system; however, in adult humans, angiogenesis only occurs as a response to a
5 pathological condition (except during the reproductive cycle in women).

Under normal physiological conditions in adults, angiogenesis takes place only in very restricted situations such as hair growth and wounding healing. Auerbach, W. and Auerbach, R., 1994, *Pharmacol Ther.* 63(3):265-311; Ribatti et al., 1991, *Haematologica* 76(4):311-20; Risau, 1997, *Nature* 386(6626):671-4. Angiogenesis progresses by a
10 stimulus which results in the formation of a migrating column of endothelial cells. Proteolytic activity is focused at the advancing tip of this "vascular sprout", which breaks down the ECM sufficiently to permit the column of cells to infiltrate and migrate. Behind the advancing front, the endothelial cells differentiate and begin to adhere to each other, thus forming a new basement membrane. The cells then cease proliferation and finally
15 define a lumen for the new arteriole or capillary.

Unregulated angiogenesis has gradually been recognized to be responsible for a wide range of disorders, including, but not limited to, cancer, cardiovascular disease, rheumatoid arthritis, psoriasis and diabetic retinopathy. Folkman, 1995, *Nat Med* 1(1):27-31; Isner, 1999, *Circulation* 99(13): 1653-5; Koch, 1998, *Arthritis Rheum* 41(6):951-62;
20 Walsh, 1999, *Rheumatology (Oxford)* 38(2):103-12; Ware and Simons, 1997, *Nat Med* 3(2): 158-64.

Of particular interest is the observation that angiogenesis is required by solid tumors for their growth and metastases. Folkman, 1986 *supra*; Folkman 1990, *J Natl. Cancer Inst.*, 82(1) 4-6; Folkman, 1992, *Semin Cancer Biol* 3(2):65-71; Zetter, 1998, *Annu*
25 *Rev Med* 49:407-24. A tumor usually begins as a single aberrant cell which can proliferate only to a size of a few cubic millimeters due to the distance from available capillary beds, and it can stay 'dormant' without further growth and dissemination for a long period of time. Some tumor cells then switch to the angiogenic phenotype to activate endothelial cells, which proliferate and mature into new capillary blood vessels. These newly formed
30 blood vessels not only allow for continued growth of the primary tumor, but also for the dissemination and recolonization of metastatic tumor cells. The precise mechanisms that control the angiogenic switch is not well understood, but it is believed that

neovascularization of tumor mass results from the net balance of a multitude of angiogenesis stimulators and inhibitors Folkman, 1995, *supra*:

One of the most potent angiogenesis inhibitors is endostatin identified by O'Reilly and Folkman. O'Reilly et al., 1997, *Cell* 88(2):277-85; O'Reilly et al., 1994, *Cell* 79(2):3
5 15-28. Its discovery was based on the phenomenon that certain primary tumors can inhibit the growth of distant metastases. O'Reilly and Folkman hypothesized that a primary tumor initiates angiogenesis by generating angiogenic stimulators in excess of inhibitors. However, angiogenic inhibitors, by virtue of their longer half life in the circulation, reach the site of a secondary tumor in excess of the stimulators. The net result is the growth of
10 primary tumor and inhibition of secondary tumor. Endostatin is one of a growing list of such angiogenesis inhibitors produced by primary tumors. It is a proteolytic fragment of a larger protein: endostatin is a 20 kDa fragment of collagen XVIII (amino acid H1132-K1315 in murine collagen XVIII). Endostatin has been shown to specifically inhibit endothelial cell proliferation in vitro and block angiogenesis in vivo. More importantly,
15 administration of endostatin to tumor-bearing mice leads to significant tumor regression, and no toxicity or drug resistance has been observed even after multiple treatment cycles. Boehm et al., 1997, *Nature* 390(6658):404-407. The fact that endostatin targets genetically stable endothelial cells and inhibits a variety of solid tumors makes it a very attractive candidate for anticancer therapy. Fidler and Ellis, 1994, *Cell* 79(2):185-8; Gastl et al.,
20 1997, *Oncology* 54(3):177-84; Hinsbergh et al., 1999, *Ann Oncol* 10 Suppl 4:60-3. In addition, angiogenesis inhibitors have been shown to be more effective when combined with radiation and chemotherapeutic agents. Klement, 2000, *J. Clin Invest*, 105(8) R15-24. Browder, 2000, *Cancer Res.* 6-(7) 1878-86, Arap et al., 1998, *Science* 279(5349):377-80; Mauceri et al., 1998, *Nature* 394(6690):287-91.

25

SUMMARY OF THE INVENTION

The present invention solves many needs in the art by providing nucleic acid molecules, polypeptides and antibodies thereto, variants and derivatives of the nucleic acids and polypeptides, and agonists and antagonists thereto that may be used to identify, diagnose, monitor, stage, image and treat colon cancer and/or non-cancerous disease states
30 in colon; identify and monitor colon tissue; and identify and design agonists and antagonists of polypeptides of the invention. The invention also provides gene therapy,

methods for producing transgenic animals and cells, and methods for producing engineered colon tissue for treatment and research.

One aspect of the present invention relates to nucleic acid molecules that are specific to colon cells, colon tissue and/or the colon organ. These colon specific nucleic acids (CSNAs) may be a naturally occurring cDNA, genomic DNA, RNA, or a fragment
5 of one of these nucleic acids, or may be a non-naturally occurring nucleic acid molecule. If the CSNA is genomic DNA, then the CSNA is a colon specific gene (CSG). If the CSNA is RNA, then it is a colon specific transcript encoded by a CSG. Due to alternative splicing and transcriptional modification one CSG may encode for multiple colon specific
10 RNAs. In a preferred embodiment, the nucleic acid molecule encodes a polypeptide that is specific to colon. More preferred is a nucleic acid molecule that encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 95-248. In another preferred embodiment, the nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1-94. For the CSNA sequences listed herein, DEX0450_001.nt.1 corresponds to SEQ ID
15 NO: 1. For sequences with multiple splice variants, the parent sequence DEX0450_001.nt.1, will be followed by DEX0450_001.nt.2, etc. for each splice variant. The sequences off the corresponding peptides are listed as DEX0450_001.aa.1, etc. For the mapping of all of the nucleotides and peptides, see the table in the Example 1 section below.

20 This aspect of the present invention also relates to nucleic acid molecules that selectively hybridize or exhibit substantial sequence similarity to nucleic acid molecules encoding a Colon Specific Protein (CSP), or that selectively hybridize or exhibit substantial sequence similarity to a CSNA. In one embodiment of the present invention the nucleic acid molecule comprises an allelic variant of a nucleic acid molecule encoding
25 a CSP, or an allelic variant of a CSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid sequence that encodes a CSP or a part of a nucleic acid sequence of a CSNA.

In addition, this aspect of the present invention relates to a nucleic acid molecule further comprising one or more expression control sequences controlling the transcription
30 and/or translation of all or a part of a CSNA or the transcription and/or translation of a nucleic acid molecule that encodes all or a fragment of a CSP.

Another aspect of the present invention relates to vectors and/or host cells comprising a nucleic acid molecule of this invention. In a preferred embodiment, the

nucleic acid molecule of the vector and/or host cell encodes all or a fragment of a CSP. In another preferred embodiment, the nucleic acid molecule of the vector and/or host cell comprises all or a part of a CSNA. Vectors and host cells of the present invention are useful in the recombinant production of polypeptides, particularly CSPs of the present invention.

Another aspect of the present invention relates to polypeptides encoded by a nucleic acid molecule of this invention. The polypeptide may comprise either a fragment or a full-length protein. In a preferred embodiment, the polypeptide is a CSP. However, this aspect of the present invention also relates to mutant proteins (muteins) of CSPs, fusion proteins of which a portion is a CSP, and proteins and polypeptides encoded by allelic variants of a CSNA as provided herein.

A further aspect of the present invention is a novel splice variant which encodes an amino acid sequence that provides a novel region to be targeted for the generation of reagents that can be used in the detection and/or treatment of cancer. The novel amino acid sequence may lead to a unique protein structure, protein subcellular localization, biochemical processing or function. This information can be used to directly or indirectly facilitate the generation of additional or novel therapeutics or diagnostics. The nucleotide sequence in this novel splice variant can be used as a nucleic acid probe for the diagnosis and/or treatment of cancer.

Another aspect of the present invention relates to antibodies and other binders that specifically bind to a polypeptide of the instant invention. Accordingly antibodies or binders of the present invention specifically bind to CSPs, muteins, fusion proteins, and/or homologous proteins or polypeptides encoded by allelic variants of a CSNA as provided herein.

Another aspect of the present invention relates to agonists and antagonists of the nucleic acid molecules and polypeptides of this invention. The agonists and antagonists of the instant invention may be used to treat colon cancer and non-cancerous disease states in colon and to produce engineered colon tissue.

Another aspect of the present invention relates to methods for using the nucleic acid molecules to detect or amplify nucleic acid molecules that have similar or identical nucleic acid sequences compared to the nucleic acid molecules described herein. Such methods are useful in identifying, diagnosing, monitoring, staging, imaging and treating colon cancer and/or non-cancerous disease states in colon. Such methods are also useful

in identifying and/or monitoring colon tissue. In addition, measurement of levels of one or more of the nucleic acid molecules of this invention may be useful as a diagnostic as part of a panel in combination with known other markers, particularly those described in the colon cancer background section above.

- 5 Another aspect of the present invention relates to use of the nucleic acid molecules of this invention in gene therapy, for producing transgenic animals and cells, and for producing engineered colon tissue for treatment and research.

- Another aspect of the present invention relates to methods for detecting polypeptides of this invention, preferably using antibodies thereto. Such methods are
10 useful to identify, diagnose, monitor, stage, image and treat colon cancer and non-cancerous disease states in colon. In addition, measurement of levels of one or more of the polypeptides of this invention may be useful to identify, diagnose, monitor, stage, and/or image colon cancer in combination with known other markers, particularly those described in the colon cancer background section above. The polypeptides of the present
15 invention can also be used to identify and/or monitor colon tissue, and to produce engineered colon tissue.

- Yet another aspect of the present invention relates to a computer readable means of storing the nucleic acid and amino acid sequences of the invention. The records of the computer readable means can be accessed for reading and displaying of sequences for
20 comparison, alignment and ordering of the sequences of the invention to other sequences. In addition, the computer records regarding the nucleic acid and/or amino acid sequences and/or measurements of their levels may be used alone or in combination with other markers to diagnose colon related diseases.

DETAILED DESCRIPTION OF THE INVENTION

25 Definitions and General Techniques

- Unless otherwise defined herein, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Generally,
30 nomenclatures used in connection with, and techniques of, cell and tissue culture, molecular biology, immunology, microbiology, genetics and protein and nucleic acid chemistry and hybridization described herein are those well known and commonly used in

the art. The methods and techniques of the present invention are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification unless otherwise indicated. *See, e.g.,* Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2d ed., Cold Spring Harbor Laboratory Press (1989) and Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 3d ed., Cold Spring Harbor Press (2001); Ausubel *et al.*, Current Protocols in Molecular Biology, Greene Publishing Associates (1992, and Supplements to 2000); Ausubel *et al.*, Short Protocols in Molecular Biology: A Compendium of Methods from Current Protocols in Molecular Biology – 4th Ed., Wiley & Sons (1999); Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press (1990); and Harlow and Lane, Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press (1999).

Enzymatic reactions and purification techniques are performed according to manufacturer's specifications, as commonly accomplished in the art or as described herein. The nomenclatures used in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well known and commonly used in the art. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

The following terms, unless otherwise indicated, shall be understood to have the following meanings:

A "nucleic acid molecule" of this invention refers to a polymeric form of nucleotides and includes both sense and antisense strands of RNA, cDNA, genomic DNA, and synthetic forms and mixed polymers of the above. A nucleotide refers to a ribonucleotide, deoxynucleotide or a modified form of either type of nucleotide. A "nucleic acid molecule" as used herein is synonymous with "nucleic acid" and "polynucleotide." The term "nucleic acid molecule" usually refers to a molecule of at least 10 bases in length, unless otherwise specified. The term includes single- and double-stranded forms of DNA. In addition, a polynucleotide may include either or both naturally occurring and modified nucleotides linked together by naturally occurring and/or non-naturally occurring nucleotide linkages.

Nucleotides are represented by single letter symbols in nucleic acid molecule sequences. The following table lists symbols identifying nucleotides or groups of

nucleotides which may occupy the symbol position on a nucleic acid molecule. *See* Nomenclature Committee of the International Union of Biochemistry (NC-IUB), Nomenclature for incompletely specified bases in nucleic acid sequences, Recommendations 1984., *Eur J Biochem.* 150(1):1-5 (1985).

Symbol	Meaning	Group/Origin of Designation	Complementary Symbol
a	a	Adenine	t/u
g	g	Guanine	c
c	c	Cytosine	g
t	t	Thymine	a
u	u	Uracil	a
r	g or a	puRine	y
y	t/u or c	pYrimidine	r
m	a or c	aMino	k
k	g or t/u	Keto	m
s	g or c	Strong interactions 3H-bonds	w
w	a or t/u	Weak interactions 2H-bonds	s
b	g or c or t/u	not a	v
d	a or g or t/u	not c	h
h	a or c or t/u	not g	d
v	a or g or c	not t, not u	b
n	a or g or c or t/u, unknown, or other	aNy	n

5

- The nucleic acid molecules may be modified chemically or biochemically or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those of skill in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages (*e.g.*, methyl phosphonates, phosphotriesters, phosphoramidates, carbamates, etc.), charged linkages (*e.g.*, phosphorothioates, phosphorodithioates, etc.), pendent moieties (*e.g.*, polypeptides), intercalators (*e.g.*, acridine, psoralen, etc.), chelators, alkylators, and modified linkages (*e.g.*, alpha anomeric nucleic acids, etc.) The term "nucleic acid molecule" also includes any topological conformation, including single-stranded, double-stranded, partially duplexed, triplexed, hairpinned, circular and padlocked conformations. Also included are synthetic molecules that mimic polynucleotides in their ability to bind to a designated sequence via hydrogen bonding and other chemical interactions. Such molecules are known in the art and include, for example, those in which peptide linkages substitute for phosphate linkages in the backbone of the molecule.

20

A "gene" is defined as a nucleic acid molecule that comprises a nucleic acid sequence that encodes a polypeptide and the expression control sequences that surround the nucleic acid sequence that encodes the polypeptide. For instance, a gene may comprise a promoter, one or more enhancers, a nucleic acid sequence that encodes a polypeptide, downstream regulatory sequences and, possibly, other nucleic acid sequences involved in regulation of the expression of an RNA. As is well known in the art, eukaryotic genes usually contain both exons and introns. The term "exon" refers to a nucleic acid sequence found in genomic DNA that is bioinformatically predicted and/or experimentally confirmed to contribute contiguous sequence to a mature mRNA transcript. The term "intron" refers to a nucleic acid sequence found in genomic DNA that is predicted and/or confirmed to not contribute to a mature mRNA transcript, but rather to be "spliced out" during processing of the transcript.

A nucleic acid molecule or polypeptide is "derived" from a particular species if the nucleic acid molecule or polypeptide has been isolated from the particular species, or if the nucleic acid molecule or polypeptide is homologous to a nucleic acid molecule or polypeptide isolated from a particular species.

An "isolated" or "substantially pure" nucleic acid or polynucleotide (*e.g.*, an RNA, DNA or a mixed polymer) is one which is substantially separated from other cellular components that naturally accompany the native polynucleotide in its natural host cell, *e.g.*, ribosomes, polymerases, or genomic sequences with which it is naturally associated. The term embraces a nucleic acid or polynucleotide that (1) has been removed from its naturally occurring environment, (2) is not associated with all or a portion of a polynucleotide in which the "isolated polynucleotide" is found in nature, (3) is operatively linked to a polynucleotide which it is not linked to in nature, (4) does not occur in nature as part of a larger sequence or (5) includes nucleotides or internucleoside bonds that are not found in nature. The term "isolated" or "substantially pure" also can be used in reference to recombinant or cloned DNA isolates, chemically synthesized polynucleotide analogs, or polynucleotide analogs that are biologically synthesized by heterologous systems. The term "isolated nucleic acid molecule" includes nucleic acid molecules that are integrated into a host cell chromosome at a heterologous site, recombinant fusions of a native fragment to a heterologous sequence, recombinant vectors present as episomes or as integrated into a host cell chromosome.

A "part" of a nucleic acid molecule refers to a nucleic acid molecule that comprises a partial contiguous sequence of at least 10 bases of the reference nucleic acid molecule. Preferably, a part comprises at least 15 to 20 bases of a reference nucleic acid molecule. In theory, a nucleic acid sequence of 17 nucleotides is of sufficient length to
5 occur at random less frequently than once in the three gigabase human genome, and thus provides a nucleic acid probe that can uniquely identify the reference sequence in a nucleic acid mixture of genomic complexity. A preferred part is one that comprises a nucleic acid sequence that can encode at least 6 contiguous amino acid sequences (fragments of at least 18 nucleotides) because they are useful in directing the expression or
10 synthesis of peptides that are useful in mapping the epitopes of the polypeptide encoded by the reference nucleic acid. *See, e.g., Geysen et al., Proc. Natl. Acad. Sci. USA* 81:3998-4002 (1984); and U.S. Patent Nos. 4,708,871 and 5,595,915, the disclosures of which are incorporated herein by reference in their entireties. A part may also comprise at least 25, 30, 35 or 40 nucleotides of a reference nucleic acid molecule, or at least 50, 60,
15 70, 80, 90, 100, 150, 200, 250, 300, 350, 400 or 500 nucleotides of a reference nucleic acid molecule. A part of a nucleic acid molecule may comprise no other nucleic acid sequences. Alternatively, a part of a nucleic acid may comprise other nucleic acid sequences from other nucleic acid molecules.

The term "oligonucleotide" refers to a nucleic acid molecule generally comprising
20 a length of 200 bases or fewer. The term often refers to single-stranded deoxyribonucleotides, but it can refer as well to single-or double-stranded ribonucleotides, RNA:DNA hybrids and double-stranded DNAs, among others. Preferably, oligonucleotides are 10 to 60 bases in length and most preferably 12, 13, 14, 15, 16, 17, 18, 19 or 20 bases in length. Other preferred oligonucleotides are 25, 30, 35, 40, 45, 50,
25 55 or 60 bases in length. Oligonucleotides may be single-stranded, *e.g.* for use as probes or primers, or may be double-stranded, *e.g.* for use in the construction of a mutant gene. Oligonucleotides of the invention can be either sense or antisense oligonucleotides. An oligonucleotide can be derivatized or modified as discussed above for nucleic acid molecules.

30 Oligonucleotides, such as single-stranded DNA probe oligonucleotides, often are synthesized by chemical methods, such as those implemented on automated oligonucleotide synthesizers. However, oligonucleotides can be made by a variety of other methods, including in vitro recombinant DNA-mediated techniques and by

expression of DNAs in cells and organisms. Initially, chemically synthesized DNAs typically are obtained without a 5' phosphate. The 5' ends of such oligonucleotides are not substrates for phosphodiester bond formation by ligation reactions that employ DNA ligases typically used to form recombinant DNA molecules. Where ligation of such
5 oligonucleotides is desired, a phosphate can be added by standard techniques, such as those that employ a kinase and ATP. The 3' end of a chemically synthesized oligonucleotide generally has a free hydroxyl group and, in the presence of a ligase, such as T4 DNA ligase, readily will form a phosphodiester bond with a 5' phosphate of another polynucleotide, such as another oligonucleotide. As is well known, this reaction can be
10 prevented selectively, where desired, by removing the 5' phosphates of the other polynucleotide(s) prior to ligation.

The term "naturally occurring nucleotide" referred to herein includes naturally occurring deoxyribonucleotides and ribonucleotides. The term "modified nucleotides" referred to herein includes nucleotides with modified or substituted sugar groups and the
15 like. The term "nucleotide linkages" referred to herein includes nucleotide linkages such as phosphorothioate, phosphorodithioate, phosphoroselenoate, phosphorodiselenoate, phosphoroanilothioate, phosphoraniladate, phosphoroamidate, and the like. *See e.g.*, LaPlanche *et al. Nucl. Acids Res.* 14:9081-9093 (1986); Stein *et al. Nucl. Acids Res.* 16:3209-3221 (1988); Zon *et al. Anti-Cancer Drug Design* 6:539-568 (1991); Zon *et al.*,
20 in Eckstein (ed.) Oligonucleotides and Analogues: A Practical Approach, pp. 87-108, Oxford University Press (1991); Uhlmann and Peyman *Chemical Reviews* 90:543 (1990), and U.S. Patent No. 5,151,510, the disclosure of which is hereby incorporated by reference in its entirety.

Unless specified otherwise, the left hand end of a polynucleotide sequence in sense
25 orientation is the 5' end and the right hand end of the sequence is the 3' end. In addition, the left hand direction of a polynucleotide sequence in sense orientation is referred to as the 5' direction, while the right hand direction of the polynucleotide sequence is referred to as the 3' direction. Further, unless otherwise indicated, each nucleotide sequence is set forth herein as a sequence of deoxyribonucleotides. It is intended, however, that the given
30 sequence be interpreted as would be appropriate to the polynucleotide composition: for example, if the isolated nucleic acid is composed of RNA, the given sequence intends ribonucleotides, with uridine substituted for thymidine.

The term "allelic variant" refers to one of two or more alternative naturally occurring forms of a gene, wherein each gene possesses a unique nucleotide sequence. In a preferred embodiment, different alleles of a given gene have similar or identical biological properties.

5 The term "percent sequence identity" in the context of nucleic acid sequences refers to the residues in two sequences which are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over a stretch of at least about nine nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about
10 32 nucleotides, and preferably at least about 36 or more nucleotides. There are a number of different algorithms known in the art which can be used to measure nucleotide sequence identity. For instance, polynucleotide sequences can be compared using FASTA, Gap or Bestfit, which are programs in Wisconsin Package Version 10.0, Genetics Computer Group (GCG), Madison, Wisconsin. FASTA, which includes, *e.g.*, the programs FASTA2
15 and FASTA3, provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson, *Methods Enzymol.* 183: 63-98 (1990); Pearson, *Methods Mol. Biol.* 132: 185-219 (2000); Pearson, *Methods Enzymol.* 266: 227-258 (1996); Pearson, *J. Mol. Biol.* 276: 71-84 (1998)). Unless otherwise specified, default parameters for a particular program or algorithm are used. For instance,
20 percent sequence identity between nucleic acid sequences can be determined using FASTA with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) or using Gap with its default parameters as provided in GCG Version 6.1.

A reference to a nucleic acid sequence encompasses its complement unless otherwise specified. Thus, a reference to a nucleic acid molecule having a particular
25 sequence should be understood to encompass its complementary strand, with its complementary sequence. The complementary strand is also useful, *e.g.*, for antisense therapy, double-stranded RNA (dsRNA) inhibition (RNAi), combination of triplex and antisense, hybridization probes and PCR primers.

In the molecular biology art, researchers use the terms "percent sequence identity",
30 "percent sequence similarity" and "percent sequence homology" interchangeably. In this application, these terms shall have the same meaning with respect to nucleic acid sequences only.

The term "substantial similarity" or "substantial sequence similarity," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 50%, more preferably 60% of the nucleotide bases, usually at least about 70%, more usually at least about 80%, preferably at least about 90%, and more preferably at least about 95-98% of the nucleotide bases, as measured by any well known algorithm of sequence identity, such as FASTA, BLAST or Gap, as discussed above.

Alternatively, substantial similarity exists between a first and second nucleic acid sequence when the first nucleic acid sequence or fragment thereof hybridizes to an antisense strand of the second nucleic acid, under selective hybridization conditions. Typically, selective hybridization will occur between the first nucleic acid sequence and an antisense strand of the second nucleic acid sequence when there is at least about 55% sequence identity between the first and second nucleic acid sequences— preferably at least about 65%, more preferably at least about 75%, and most preferably at least about 90% — over a stretch of at least about 14 nucleotides, more preferably at least 17 nucleotides, even more preferably at least 20, 25, 30, 35, 40, 50, 60, 70, 80, 90 or 100 nucleotides.

Nucleic acid hybridization will be affected by such conditions as salt concentration, temperature, solvents, the base composition of the hybridizing species, length of the complementary regions, and the number of nucleotide base mismatches between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art. "Stringent hybridization conditions" and "stringent wash conditions" in the context of nucleic acid hybridization experiments depend upon a number of different physical parameters. The most important parameters include temperature of hybridization, base composition of the nucleic acids, salt concentration and length of the nucleic acid. One having ordinary skill in the art knows how to vary these parameters to achieve a particular stringency of hybridization. In general, "stringent hybridization" is performed at about 25°C below the thermal melting point (T_m) for the specific DNA hybrid under a particular set of conditions. "Stringent washing" is performed at temperatures about 5°C lower than the T_m for the specific DNA hybrid under a particular set of conditions. The T_m is the temperature at which 50% of the target sequence hybridizes to a perfectly matched probe. See Sambrook (1989), *supra*, p. 9.51.

The T_m for a particular DNA-DNA hybrid can be estimated by the formula:

$T_m = 81.5^{\circ}\text{C} + 16.6 (\log_{10}[\text{Na}^+]) + 0.41 (\text{fraction G} + \text{C}) - 0.63 (\% \text{ formamide}) - (600/l)$ where l is the length of the hybrid in base pairs.

The T_m for a particular RNA-RNA hybrid can be estimated by the formula:

$T_m = 79.8^{\circ}\text{C} + 18.5 (\log_{10}[\text{Na}^+]) + 0.58 (\text{fraction G} + \text{C}) +$

5 $11.8 (\text{fraction G} + \text{C})^2 - 0.35 (\% \text{ formamide}) - (820/l).$

The T_m for a particular RNA-DNA hybrid can be estimated by the formula:

$T_m = 79.8^{\circ}\text{C} + 18.5 (\log_{10}[\text{Na}^+]) + 0.58 (\text{fraction G} + \text{C}) +$

$11.8 (\text{fraction G} + \text{C})^2 - 0.50 (\% \text{ formamide}) - (820/l).$

In general, the T_m decreases by 1-1.5°C for each 1% of mismatch between two
 10 nucleic acid sequences. Thus, one having ordinary skill in the art can alter hybridization and/or washing conditions to obtain sequences that have higher or lower degrees of sequence identity to the target nucleic acid. For instance, to obtain hybridizing nucleic acids that contain up to 10% mismatch from the target nucleic acid sequence, 10-15°C would be subtracted from the calculated T_m of a perfectly matched hybrid, and then the
 15 hybridization and washing temperatures adjusted accordingly. Probe sequences may also hybridize specifically to duplex DNA under certain conditions to form triplex or other higher order DNA complexes. The preparation of such probes and suitable hybridization conditions are well known in the art.

An example of stringent hybridization conditions for hybridization of
 20 complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or Northern blot or for screening a library is 50% formamide/6X SSC at 42°C for at least ten hours and preferably overnight (approximately 16 hours). Another example of stringent hybridization conditions is 6X SSC at 68°C without formamide for at least ten hours and preferably overnight. An example of moderate stringency
 25 hybridization conditions is 6X SSC at 55°C without formamide for at least ten hours and preferably overnight. An example of low stringency hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or northern blot or for screening a library is 6X SSC at 42°C for at least ten hours. Hybridization conditions to identify nucleic acid
 30 sequences that are similar but not identical can be identified by experimentally changing the hybridization temperature from 68°C to 42°C while keeping the salt concentration constant (6X SSC), or keeping the hybridization temperature and salt concentration constant (e.g. 42°C and 6X SSC) and varying the formamide concentration from 50% to

0%. Hybridization buffers may also include blocking agents to lower background. These agents are well known in the art. *See* Sambrook *et al.* (1989), *supra*, pages 8.46 and 9.46-9.58. *See also* Ausubel (1992), *supra*, Ausubel (1999), *supra*, and Sambrook (2001), *supra*.

- 5 Wash conditions also can be altered to change stringency conditions. An example of stringent wash conditions is a 0.2x SSC wash at 65°C for 15 minutes (*see* Sambrook (1989), *supra*, for SSC buffer). Often the high stringency wash is preceded by a low stringency wash to remove excess probe. An exemplary medium stringency wash for duplex DNA of more than 100 base pairs is 1x SSC at 45°C for 15 minutes. An
10 exemplary low stringency wash for such a duplex is 4x SSC at 40°C for 15 minutes. In general, signal-to-noise ratio of 2x or higher than that observed for an unrelated probe in the particular hybridization assay indicates detection of a specific hybridization.

- As defined herein, nucleic acids that do not hybridize to each other under stringent conditions are still substantially similar to one another if they encode polypeptides that are
15 substantially identical to each other. This occurs, for example, when a nucleic acid is created synthetically or recombinantly using a high codon degeneracy as permitted by the redundancy of the genetic code.

- Hybridization conditions for nucleic acid molecules that are shorter than 100 nucleotides in length (*e.g.*, for oligonucleotide probes) may be calculated by the formula:
20 $T_m = 81.5^{\circ}\text{C} + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\text{fraction G+C}) - (600/\text{N})$, wherein N is change length and the $[\text{Na}^+]$ is 1 M or less. *See* Sambrook (1989), *supra*, p. 11.46. For hybridization of probes shorter than 100 nucleotides, hybridization is usually performed under stringent conditions (5-10°C below the T_m) using high concentrations (0.1-1.0 pmol/ml) of probe. *Id.* at p. 11.45. Determination of hybridization using mismatched
25 probes, pools of degenerate probes or “guessmers,” as well as hybridization solutions and methods for empirically determining hybridization conditions are well known in the art. *See, e.g.*, Ausubel (1999), *supra*; Sambrook (1989), *supra*, pp. 11.45-11.57.

- The term “digestion” or “digestion of DNA” refers to catalytic cleavage of the DNA with a restriction enzyme that acts only at certain sequences in the DNA. The
30 various restriction enzymes referred to herein are commercially available and their reaction conditions, cofactors and other requirements for use are known and routine to the skilled artisan. For analytical purposes, typically, 1 µg of plasmid or DNA fragment is digested with about 2 units of enzyme in about 20 µl of reaction buffer. For the purpose of

isolating DNA fragments for plasmid construction, typically 5 to 50 μ g of DNA are digested with 20 to 250 units of enzyme in proportionately larger volumes. Appropriate buffers and substrate amounts for particular restriction enzymes are described in standard laboratory manuals, such as those referenced below, and are specified by commercial
5 suppliers. Incubation times of about 1 hour at 37°C are ordinarily used, but conditions may vary in accordance with standard procedures, the supplier's instructions and the particulars of the reaction. After digestion, reactions may be analyzed, and fragments may be purified by electrophoresis through an agarose or polyacrylamide gel, using well known methods that are routine for those skilled in the art.

10 The term "ligation" refers to the process of forming phosphodiester bonds between two or more polynucleotides, which most often are double-stranded DNAs. Techniques for ligation are well known to the art and protocols for ligation are described in standard laboratory manuals and references, such as, *e.g.*, Sambrook (1989), *supra*.

Genome-derived "single exon probes," are probes that comprise at least part of an
15 exon ("reference exon") and can hybridize detectably under high stringency conditions to transcript-derived nucleic acids that include the reference exon but do not hybridize detectably under high stringency conditions to nucleic acids that lack the reference exon. Single exon probes typically further comprise, contiguous to a first end of the exon portion, a first intronic and/or intergenic sequence that is identically contiguous to the
20 exon in the genome, and may contain a second intronic and/or intergenic sequence that is identically contiguous to the exon in the genome. The minimum length of genome-derived single exon probes is defined by the requirement that the exonic portion be of sufficient length to hybridize under high stringency conditions to transcript-derived nucleic acids, as discussed above. The maximum length of genome-derived single exon
25 probes is defined by the requirement that the probes contain portions of no more than one exon. The single exon probes may contain priming sequences not found in contiguity with the rest of the probe sequence in the genome, which priming sequences are useful for PCR and other amplification-based technologies. In another aspect, the invention is directed to single exon probes based on the CSNAs disclosed herein.

30 In one embodiment, the term "microarray" refers to a "nucleic acid microarray" having a substrate-bound plurality of nucleic acids, hybridization to each of the plurality of bound nucleic acids being separately detectable. The substrate can be solid or porous, planar or non-planar, unitary or distributed. Nucleic acid microarrays include all the

devices so called in Schena (ed.), DNA Microarrays: A Practical Approach (Practical Approach Series), Oxford University Press (1999); *Nature Genet.* 21(1)(suppl.):1 - 60 (1999); Schena (ed.), Microarray Biochip: Tools and Technology, Eaton Publishing Company/BioTechniques Books Division (2000). Additionally, these nucleic acid

5 microarrays include a substrate-bound plurality of nucleic acids in which the plurality of nucleic acids are disposed on a plurality of beads, rather than on a unitary planar substrate, as is described, *inter alia*, in Brenner *et al.*, *Proc. Natl. Acad. Sci. USA* 97(4):1665-1670 (2000). Examples of nucleic acid microarrays may be found in U.S. Patent Nos.

6,391,623, 6,383,754, 6,383,749, 6,380,377, 6,379,897, 6,376,191, 6,372,431, 6,351,712

10 6,344,316, 6,316,193, 6,312,906, 6,309,828, 6,309,824, 6,306,643, 6,300,063, 6,287,850, 6,284,497, 6,284,465, 6,280,954, 6,262,216, 6,251,601, 6,245,518, 6,263,287, 6,251,601, 6,238,866, 6,228,575, 6,214,587, 6,203,989, 6,171,797, 6,103,474, 6,083,726, 6,054,274, 6,040,138, 6,083,726, 6,004,755, 6,001,309, 5,958,342, 5,952,180, 5,936,731, 5,843,655, 5,814,454, 5,837,196, 5,436,327, 5,412,087, and 5,405,783, the disclosures of which are

15 incorporated herein by reference in their entireties.

In an alternative embodiment, a "microarray" may also refer to a "peptide microarray" or "protein microarray" having a substrate-bound collection or plurality of polypeptides, the binding to each of the plurality of bound polypeptides being separately detectable. Alternatively, the peptide microarray may have a plurality of binders,

20 including but not limited to monoclonal antibodies, polyclonal antibodies, phage display binders, yeast 2 hybrid binders, and aptamers, which can specifically detect the binding of the polypeptides of this invention. The array may be based on autoantibody detection to the polypeptides of this invention, see Robinson *et al.*, *Nature Medicine* 8(3):295-301 (2002). Examples of peptide arrays may be found in WO 02/31463, WO 02/25288, WO

25 01/94946, WO 01/88162, WO 01/68671, WO 01/57259, WO 00/61806, WO 00/54046, WO 00/47774, WO 99/40434, WO 99/39210, and WO 97/42507 and U.S. Patent Nos. 6,268,210, 5,766,960, and 5,143,854, the disclosures of which are incorporated herein by reference in their entireties.

In addition, determination of the levels of the CSNA or CSP may be made in a

30 multiplex manner using techniques described in WO 02/29109, WO 02/24959, WO 01/83502, WO01/73113, WO 01/59432, WO 01/57269, and WO 99/67641, the disclosures of which are incorporated herein by reference in their entireties.

The term "mutant", "mutated", or "mutation" when applied to nucleic acid sequences means that nucleotides in a nucleic acid sequence may be inserted, deleted or changed compared to a reference nucleic acid sequence. A single alteration may be made at a locus (a point mutation) or multiple nucleotides may be inserted, deleted or changed at a single locus. In addition, one or more alterations may be made at any number of loci within a nucleic acid sequence. In a preferred embodiment of the present invention, the nucleic acid sequence is the wild type nucleic acid sequence encoding a CSP or is a CSNA. The nucleic acid sequence may be mutated by any method known in the art including those mutagenesis techniques described *infra*.

10 The term "error-prone PCR" refers to a process for performing PCR under conditions where the copying fidelity of the DNA polymerase is low, such that a high rate of point mutations is obtained along the entire length of the PCR product. *See, e.g., Leung et al., Technique 1: 11-15 (1989) and Caldwell et al., PCR Methods Applic. 2: 28-33 (1992).*

15 The term "oligonucleotide-directed mutagenesis" refers to a process which enables the generation of site-specific mutations in any cloned DNA segment of interest. *See, e.g., Reidhaar-Olson et al., Science 241: 53-57 (1988).*

The term "assembly PCR" refers to a process which involves the assembly of a PCR product from a mixture of small DNA fragments. A large number of different PCR reactions occur in parallel in the same vial, with the products of one reaction priming the products of another reaction.

20 The term "sexual PCR mutagenesis" or "DNA shuffling" refers to a method of error-prone PCR coupled with forced homologous recombination between DNA molecules of different but highly related DNA sequence *in vitro*, caused by random fragmentation of the DNA molecule based on sequence similarity, followed by fixation of the crossover by primer extension in an error-prone PCR reaction. *See, e.g., Stemmer, Proc. Natl. Acad. Sci. U.S.A. 91: 10747-10751 (1994).* DNA shuffling can be carried out between several related genes ("Family shuffling").

25 The term "*in vivo* mutagenesis" refers to a process of generating random mutations in any cloned DNA of interest which involves the propagation of the DNA in a strain of bacteria such as *E. coli* that carries mutations in one or more of the DNA repair pathways. These "mutator" strains have a higher random mutation rate than that of a wild-type

parent. Propagating the DNA in a mutator strain will eventually generate random mutations within the DNA.

The term "cassette mutagenesis" refers to any process for replacing a small region of a double-stranded DNA molecule with a synthetic oligonucleotide "cassette" that
5 differs from the native sequence. The oligonucleotide often contains completely and/or partially randomized native sequence.

The term "recursive ensemble mutagenesis" refers to an algorithm for protein engineering (protein mutagenesis) developed to produce diverse populations of phenotypically related mutants whose members differ in amino acid sequence. This
10 method uses a feedback mechanism to control successive rounds of combinatorial cassette mutagenesis. *See, e.g., Arkin et al., Proc. Natl. Acad. Sci. U.S.A.* 89: 7811-7815 (1992).

The term "exponential ensemble mutagenesis" refers to a process for generating combinatorial libraries with a high percentage of unique and functional mutants, wherein small groups of residues are randomized in parallel to identify, at each altered position,
15 amino acids which lead to functional proteins. *See, e.g., Delegrave et al., Biotechnology Research* 11: 1548-1552 (1993); Arnold, *Current Opinion in Biotechnology* 4: 450-455 (1993).

"Operatively linked" expression control sequences refers to a linkage in which the expression control sequence is either contiguous with the gene of interest to control the
20 gene of interest, or acts in *trans* or at a distance to control the gene of interest.

The term "expression control sequence" as used herein refers to polynucleotide sequences which are necessary to affect the expression of coding sequences to which they are operatively linked. Expression control sequences are sequences which control the transcription, post-transcriptional events and translation of nucleic acid sequences.
25 Expression control sequences include appropriate transcription initiation, termination, promoter and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (*e.g.,* ribosome binding sites); sequences that enhance protein stability; and when desired, sequences that enhance protein secretion. The nature
30 of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include promoter, ribosomal binding site, and transcription termination sequence. The term "control sequences" is intended to include, at a minimum, all components whose presence is essential for expression, and can also include additional

components whose presence is advantageous, for example, leader sequences and fusion partner sequences.

The term "vector," as used herein, is intended to refer to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of
5 vector is a "plasmid", which refers to a circular double-stranded DNA loop into which additional DNA segments may be ligated. Other vectors include cosmids, bacterial artificial chromosomes (BAC) and yeast artificial chromosomes (YAC). Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome. Viral vectors that infect bacterial cells are referred to as bacteriophages. Certain
10 vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication). Other vectors can be integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are
15 referred to herein as "recombinant expression vectors" (or simply, "expression vectors"). In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" may be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include other forms of expression vectors that serve equivalent
20 functions.

The term "recombinant host cell" (or simply "host cell"), as used herein, is intended to refer to a cell into which a recombinant expression vector has been introduced. It should be understood that such terms are intended to refer not only to the particular subject cell but to the progeny of such a cell. Because certain modifications may occur in
25 succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term "host cell" as used herein.

As used herein, the phrase "open reading frame" and the equivalent acronym "ORF" refers to that portion of a transcript-derived nucleic acid that can be translated in its
30 entirety into a sequence of contiguous amino acids. As so defined, an ORF has length, measured in nucleotides, exactly divisible by 3. As so defined, an ORF need not encode the entirety of a natural protein.

As used herein, the phrase "ORF-encoded peptide" refers to the predicted or actual translation of an ORF.

As used herein, the phrase "degenerate variant" of a reference nucleic acid sequence is meant to be inclusive of all nucleic acid sequences that can be directly
5 translated, using the standard genetic code, to provide an amino acid sequence identical to that translated from the reference nucleic acid sequence.

The term "polypeptide" encompasses both naturally occurring and non-naturally occurring proteins and polypeptides, as well as polypeptide fragments and polypeptide mutants, derivatives and analogs thereof. A polypeptide may be monomeric or polymeric.
10 Further, a polypeptide may comprise a number of different modules within a single polypeptide each of which has one or more distinct activities. A preferred polypeptide in accordance with the invention comprises a CSP encoded by a nucleic acid molecule of the instant invention, or a fragment, mutant, analog or derivative thereof.

The term "isolated protein" or "isolated polypeptide" is a protein or polypeptide
15 that by virtue of its origin or source of derivation (1) is not associated with naturally associated components that accompany it in its native state, (2) is free of other proteins from the same species (3) is expressed by a cell from a different species, or (4) does not occur in nature. Thus, a polypeptide that is chemically synthesized or synthesized in a cellular system different from the cell from which it naturally originates will be "isolated"
20 from its naturally associated components. A polypeptide or protein may also be rendered substantially free of naturally associated components by isolation, using protein purification techniques well known in the art.

A protein or polypeptide is "substantially pure," "substantially homogeneous" or "substantially purified" when at least about 60% to 75% of a sample exhibits a single
25 species of polypeptide. The polypeptide or protein may be monomeric or multimeric. A substantially pure polypeptide or protein will typically comprise about 50%, 60%, 70%, 80% or 90% W/W of a protein sample, more usually about 95%, and preferably will be over 99% pure. Protein purity or homogeneity may be determined by a number of means well known in the art, such as polyacrylamide gel electrophoresis of a protein sample,
30 followed by visualizing a single polypeptide band upon staining the gel with a stain well known in the art. For certain purposes, higher resolution may be provided by using HPLC or other means well known in the art for purification.

The term "fragment" when used herein with respect to polypeptides of the present invention refers to a polypeptide that has an amino-terminal and/or carboxy-terminal deletion compared to a full-length CSP. In a preferred embodiment, the fragment is a contiguous sequence in which the amino acid sequence of the fragment is identical to the corresponding positions in the naturally occurring polypeptide. Fragments typically are at least 5, 6, 7, 8, 9 or 10 amino acids long, preferably at least 12, 14, 16 or 18 amino acids long, more preferably at least 20 amino acids long, more preferably at least 25, 30, 35, 40 or 45, amino acids, even more preferably at least 50 or 60 amino acids long, and even more preferably at least 70 amino acids long.

A "derivative" when used herein with respect to polypeptides of the present invention refers to a polypeptide which is substantially similar in primary structural sequence to a CSP but which includes, *e.g.*, *in vivo* or *in vitro* chemical and biochemical modifications that are not found in the CSP. Such modifications include, for example, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. Other modifications include, *e.g.*, labeling with radionuclides, and various enzymatic modifications, as will be readily appreciated by those skilled in the art. A variety of methods for labeling polypeptides and of substituents or labels useful for such purposes are well known in the art, and include radioactive isotopes such as ^{125}I , ^{32}P , ^{35}S , ^{14}C and ^3H , ligands which bind to labeled antiligands (*e.g.*, antibodies), fluorophores, chemiluminescent agents, enzymes, and antiligands which can serve as specific binding pair members for a labeled ligand. The choice of label depends on the sensitivity required, ease of conjugation with the primer, stability requirements, and available instrumentation. Methods for labeling polypeptides are well known in the art. *See* Ausubel (1992), *supra*; Ausubel (1999), *supra*.

The term "fusion protein" refers to polypeptides of the present invention coupled to a heterologous amino acid sequence. Fusion proteins are useful because they can be constructed to contain two or more desired functional elements from two or more different proteins. A fusion protein comprises at least 10 contiguous amino acids from a polypeptide of interest, more preferably at least 20 or 30 amino acids, even more preferably at least 40, 50 or 60 amino acids, yet more preferably at least 75, 100 or 125 amino acids. Fusion proteins can be produced recombinantly by constructing a nucleic acid sequence that encodes the polypeptide or a fragment thereof in frame with a nucleic acid sequence encoding a different protein or peptide and then expressing the fusion protein. Alternatively, a fusion protein can be produced chemically by crosslinking the polypeptide or a fragment thereof to another protein.

The term "analog" refers to both polypeptide analogs and non-peptide analogs. The term "polypeptide analog" as used herein refers to a polypeptide that is comprised of a segment of at least 25 amino acids that has substantial identity to a portion of an amino acid sequence but which contains non-natural amino acids or non-natural inter-residue bonds. In a preferred embodiment, the analog has the same or similar biological activity as the native polypeptide. Typically, polypeptide analogs comprise a conservative amino acid substitution (or insertion or deletion) with respect to the naturally occurring sequence. Analogs typically are at least 20 amino acids long, preferably at least 50 amino acids long or longer, and can often be as long as a full-length naturally occurring polypeptide.

The term "non-peptide analog" refers to a compound with properties that are analogous to those of a reference polypeptide. A non-peptide compound may also be termed a "peptide mimetic" or a "peptidomimetic." Such compounds are often developed with the aid of computerized molecular modeling. Peptide mimetics that are structurally similar to useful peptides may be used to produce an equivalent effect. Generally, peptidomimetics are structurally similar to a paradigm polypeptide (*i.e.*, a polypeptide that has a desired biochemical property or pharmacological activity), but have one or more peptide linkages optionally replaced by a linkage selected from the group consisting of: --CH₂NH--, --CH₂S--, --CH₂-CH₂--, --CH=CH--(cis and trans), --COCH₂--, --CH(OH)CH₂--, and --CH₂SO--, by methods well known in the art. Systematic substitution of one or more amino acids of a consensus sequence with a D-amino acid of the same type (*e.g.*, D-lysine in place of L-lysine) may also be used to generate more

stable peptides. In addition, constrained peptides comprising a consensus sequence or a substantially identical consensus sequence variation may be generated by methods known in the art (Rizo *et al.*, *Ann. Rev. Biochem.* 61:387-418 (1992)). For example, one may add internal cysteine residues capable of forming intramolecular disulfide bridges which
5 cyclize the peptide.

The term "mutant" or "mutein" when referring to a polypeptide of the present invention relates to an amino acid sequence containing substitutions, insertions or deletions of one or more amino acids compared to the amino acid sequence of a CSP. A mutein may have one or more amino acid point substitutions, in which a single amino acid
10 at a position has been changed to another amino acid, one or more insertions and/or deletions, in which one or more amino acids are inserted or deleted, respectively, in the sequence of the naturally occurring protein, and/or truncations of the amino acid sequence at either or both the amino or carboxy termini. Further, a mutein may have the same or different biological activity as the naturally occurring protein. For instance, a mutein may
15 have an increased or decreased biological activity. A mutein has at least 50% sequence similarity to the wild type protein, preferred is 60% sequence similarity, more preferred is 70% sequence similarity. Even more preferred are muteins having 80%, 85% or 90% sequence similarity to a CSP. In an even more preferred embodiment, a mutein exhibits 95% sequence identity, even more preferably 97%, even more preferably 98% and even
20 more preferably 99%. Sequence similarity may be measured by any common sequence analysis algorithm, such as GAP or BESTFIT or other variation Smith-Waterman alignment. *See*, T. F. Smith and M. S. Waterman, *J. Mol. Biol.* 147:195-197 (1981) and W.R. Pearson, *Genomics* 11:635-650 (1991).

Preferred amino acid substitutions are those which: (1) reduce susceptibility to
25 proteolysis, (2) reduce susceptibility to oxidation, (3) alter binding affinity for forming protein complexes, (4) alter binding affinity or enzymatic activity, and (5) confer or modify other physicochemical or functional properties of such analogs. For example, single or multiple amino acid substitutions (preferably conservative amino acid substitutions) may be made in the naturally occurring sequence (preferably in the portion
30 of the polypeptide outside the domain(s) forming intermolecular contacts. In a preferred embodiment, the amino acid substitutions are moderately conservative substitutions or conservative substitutions. In a more preferred embodiment, the amino acid substitutions are conservative substitutions. A conservative amino acid substitution should not

substantially change the structural characteristics of the parent sequence (*e.g.*, a replacement amino acid should not tend to disrupt a helix that occurs in the parent sequence, or disrupt other types of secondary structure that characterize the parent sequence). Examples of art-recognized polypeptide secondary and tertiary structures are described in Creighton (ed.), Proteins, Structures and Molecular Principles, W. H. Freeman and Company (1984); Branden *et al.* (ed.), Introduction to Protein Structure, Garland Publishing (1991); Thornton *et al.*, *Nature* 354:105-106 (1991).

As used herein, the twenty conventional amino acids and their abbreviations follow conventional usage. See Golub *et al.* (eds.), Immunology - A Synthesis 2nd Ed., Sinauer Associates (1991). Stereoisomers (*e.g.*, D-amino acids) of the twenty conventional amino acids, unnatural amino acids such as α -, α -disubstituted amino acids, N-alkyl amino acids, and other unconventional amino acids may also be suitable components for polypeptides of the present invention. Examples of unconventional amino acids include: 4-hydroxyproline, γ -carboxyglutamate, ϵ -N,N,N-trimethyllysine, ϵ -N-acetyllysine, O-phosphoserine, N-acetylserine, N-formylmethionine, 3-methylhistidine, 5-hydroxylysine, s-N-methylarginine, and other similar amino acids and imino acids (*e.g.*, 4-hydroxyproline). In the polypeptide notation used herein, the lefthand direction is the amino terminal direction and the right hand direction is the carboxy-terminal direction, in accordance with standard usage and convention.

By "homology" or "homologous" when referring to a polypeptide of the present invention it is meant polypeptides from different organisms with a similar sequence to the encoded amino acid sequence of a CSP and a similar biological activity or function. Although two polypeptides are said to be "homologous," this does not imply that there is necessarily an evolutionary relationship between the polypeptides. Instead, the term "homologous" is defined to mean that the two polypeptides have similar amino acid sequences and similar biological activities or functions. In a preferred embodiment, a homologous polypeptide is one that exhibits 50% sequence similarity to CSP, preferred is 60% sequence similarity, more preferred is 70% sequence similarity. Even more preferred are homologous polypeptides that exhibit 80%, 85% or 90% sequence similarity to a CSP. In yet a more preferred embodiment, a homologous polypeptide exhibits 95%, 97%, 98% or 99% sequence similarity.

When "sequence similarity" is used in reference to polypeptides, it is recognized that residue positions that are not identical often differ by conservative amino acid

substitutions. In a preferred embodiment, a polypeptide that has "sequence similarity" comprises conservative or moderately conservative amino acid substitutions. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well known to those of skill in the art. See, e.g., Pearson, *Methods Mol. Biol.* 24: 307-31 (1994).

For instance, the following six groups each contain amino acids that are conservative substitutions for one another:

- 1) Serine (S), Threonine (T);
- 2) Aspartic Acid (D), Glutamic Acid (E);
- 3) Asparagine (N), Glutamine (Q);
- 4) Arginine (R), Lysine (K);
- 5) Isoleucine (I), Leucine (L), Methionine (M), Alanine (A), Valine (V), and
- 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W).

Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet *et al.*, *Science* 256: 1443-45 (1992). A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

Sequence similarity for polypeptides, which is also referred to as sequence identity, is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG contains programs such as "Gap" and "Bestfit" which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organisms or between a wild type protein and a mutein thereof. See, e.g., GCG Version 6.1. Other programs include FASTA, discussed *supra*.

A preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program BLAST, especially blastp or tblastn. See, e.g., Altschul *et al.*, *J. Mol. Biol.* 215: 403-410 (1990); Altschul *et al.*, *Nucleic Acids Res.* 25:3389-402 (1997). Preferred parameters for

blastp are:

Expectation value:	10 (default)
Filter:	seg (default)
Cost to open a gap:	11 (default)
Cost to extend a gap:	1 (default)
Max. alignments:	100 (default)
Word size:	11 (default)
No. of descriptions:	100 (default)
Penalty Matrix:	BLOSUM62

The length of polypeptide sequences compared for homology will generally be at least about 16 amino acid residues, usually at least about 20 residues, more usually at least about 24 residues, typically at least about 28 residues, and preferably more than about 35 residues. When searching a database containing sequences from a large number of different organisms, it is preferable to compare amino acid sequences.

Algorithms other than blastp for database searching using amino acid sequences are known in the art. For instance, polypeptide sequences can be compared using FASTA, a program in GCG Version 6.1. FASTA (e.g., FASTA2 and FASTA3) provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (1990), *supra*; Pearson (2000), *supra*. For example, percent sequence identity between amino acid sequences can be determined using FASTA with its default or recommended parameters (a word size of 2 and the PAM250 scoring matrix), as provided in GCG Version 6.1.

An "antibody" refers to an intact immunoglobulin, or to an antigen-binding portion thereof that competes with the intact antibody for specific binding to a molecular species, e.g., a polypeptide of the instant invention. Antigen-binding portions may be produced by recombinant DNA techniques or by enzymatic or chemical cleavage of intact antibodies. Antigen-binding portions include, *inter alia*, Fab, Fab', F(ab')₂, Fv, dAb, and complementarity determining region (CDR) fragments, single-chain antibodies (scFv), chimeric antibodies, diabodies and polypeptides that contain at least a portion of an

immunoglobulin that is sufficient to confer specific antigen binding to the polypeptide. A Fab fragment is a monovalent fragment consisting of the VL, VH, CL and CH1 domains; a F(ab')₂ fragment is a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consists of the VH and CH1 domains; a
5 Fv fragment consists of the VL and VH domains of a single arm of an antibody; and a dAb fragment consists of a VH domain. *See, e.g., Ward et al., Nature* 341: 544-546 (1989).

By "bind specifically" and "specific binding" as used herein it is meant the ability of the antibody to bind to a first molecular species in preference to binding to other molecular species with which the antibody and first molecular species are admixed. An
10 antibody is said to "recognize" a first molecular species when it can bind specifically to that first molecular species.

A single-chain antibody (scFv) is an antibody in which VL and VH regions are paired to form a monovalent molecule via a synthetic linker that enables them to be made as a single protein chain. *See, e.g., Bird et al., Science* 242: 423-426 (1988); Huston *et al.,*
15 *Proc. Natl. Acad. Sci. USA* 85: 5879-5883 (1988). Diabodies are bivalent, bispecific antibodies in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with complementary domains of another chain and creating two antigen binding sites. *See e.g., Holliger et al., Proc. Natl. Acad. Sci. USA*
20 90: 6444-6448 (1993); Poljak *et al., Structure* 2: 1121-1123 (1994). One or more CDRs may be incorporated into a molecule either covalently or noncovalently to make it an immunoadhesin. An immunoadhesin may incorporate the CDR(s) as part of a larger polypeptide chain, may covalently link the CDR(s) to another polypeptide chain, or may incorporate the CDR(s) noncovalently. The CDRs permit the immunoadhesin to
25 specifically bind to a particular antigen of interest. A chimeric antibody is an antibody that contains one or more regions from one antibody and one or more regions from one or more other antibodies.

An antibody may have one or more binding sites. If there is more than one binding site, the binding sites may be identical to one another or may be different. For instance, a
30 naturally occurring immunoglobulin has two identical binding sites, a single-chain antibody or Fab fragment has one binding site, while a "bispecific" or "bifunctional" antibody has two different binding sites.

An "isolated antibody" is an antibody that (1) is not associated with naturally-associated components, including other naturally-associated antibodies, that accompany it in its native state, (2) is free of other proteins from the same species, (3) is expressed by a cell from a different species, or (4) does not occur in nature. It is known that purified
5 proteins, including purified antibodies, may be stabilized with non-naturally-associated components. The non-naturally-associated component may be a protein, such as albumin (*e.g.*, BSA) or a chemical such as polyethylene glycol (PEG).

A "neutralizing antibody" or "an inhibitory antibody" is an antibody that inhibits the activity of a polypeptide or blocks the binding of a polypeptide to a ligand that
10 normally binds to it. An "activating antibody" is an antibody that increases the activity of a polypeptide.

The term "epitope" includes any protein determinant capable of specific binding to an immunoglobulin or T-cell receptor. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains
15 and usually have specific three-dimensional structural characteristics, as well as specific charge characteristics. An antibody is said to specifically bind an antigen when the dissociation constant is less than 1 μ M, preferably less than 100 nM and most preferably less than 10 nM.

The term "patient" includes human and veterinary subjects.

20 Throughout this specification and claims, the word "comprise," or variations such as "comprises" or "comprising," will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

The term "colon specific" refers to a nucleic acid molecule or polypeptide that is expressed predominantly in the colon as compared to other tissues in the body. In a preferred embodiment, a "colon specific" nucleic acid molecule or polypeptide is detected
25 at a level that is 1.5-fold higher than any other tissue in the body. In a more preferred embodiment, the "colon specific" nucleic acid molecule or polypeptide is detected at a level that is 2-fold higher than any other tissue in the body, more preferably 5-fold higher, still more preferably at least 10-fold, 15-fold, 20-fold, 25-fold, 50-fold or 100-fold higher
30 than any other tissue in the body. Nucleic acid molecule levels may be measured by nucleic acid hybridization, such as Northern blot hybridization, or quantitative PCR. Polypeptide levels may be measured by any method known to accurately quantitate protein levels, such as Western blot analysis.

Nucleic Acid Molecules, Regulatory Sequences, Vectors, Host Cells and Recombinant
Methods of Making Polypeptides

Nucleic Acid Molecules

One aspect of the invention provides isolated nucleic acid molecules that are
5 specific to the colon or to colon cells or tissue or that are derived from such nucleic acid
molecules. These isolated colon specific nucleic acids (CSNAs) may comprise cDNA
genomic DNA, RNA, or a combination thereof, a fragment of one of these nucleic acids,
or may be a non-naturally occurring nucleic acid molecule. A CSNA may be derived from
an animal. In a preferred embodiment, the CSNA is derived from a human or other
10 mammal. In a more preferred embodiment, the CSNA is derived from a human or other
primate. In an even more preferred embodiment, the CSNA is derived from a human.

In a preferred embodiment, the nucleic acid molecule encodes a polypeptide that
is specific to colon, a colon-specific polypeptide (CSP). In a more preferred embodiment,
the nucleic acid molecule encodes a polypeptide that comprises an amino acid sequence of
15 SEQ ID NO: 95-248. In another highly preferred embodiment, the nucleic acid molecule
comprises a nucleic acid sequence of SEQ ID NO: 1-94. Nucleotide sequences of the
instantly-described nucleic acid molecules were determined by assembling several DNA
molecules from either public or proprietary databases. Some of the underlying DNA
sequences are the result, directly or indirectly, of at least one enzymatic polymerization
20 reaction (*e.g.*, reverse transcription and/or polymerase chain reaction) using an automated
sequencer (such as the MegaBACE™ 1000, Amersham Biosciences, Sunnyvale, CA,
USA).

Nucleic acid molecules of the present invention may also comprise sequences that
selectively hybridize to a nucleic acid molecule encoding a CSNA or a complement or
25 antisense thereof. The hybridizing nucleic acid molecule may or may not encode a
polypeptide or may or may not encode a CSP. However, in a preferred embodiment, the
hybridizing nucleic acid molecule encodes a CSP. In a more preferred embodiment, the
invention provides a nucleic acid molecule that selectively hybridizes to a nucleic acid
molecule or the antisense sequence of a nucleic acid molecule that encodes a polypeptide
30 comprising an amino acid sequence of SEQ ID NO: 95-248. In an even more preferred
embodiment, the invention provides a nucleic acid molecule that selectively hybridizes to
a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1-94 or the
antisense sequence thereof. Preferably, the nucleic acid molecule selectively hybridizes to

a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a CSP under low stringency conditions. More preferably, the nucleic acid molecule selectively hybridizes to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a CSP under moderate stringency conditions. Most preferably, the nucleic acid molecule selectively hybridizes to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a CSP under high stringency conditions. In a preferred embodiment, the nucleic acid molecule hybridizes under low, moderate or high stringency conditions to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence of SEQ ID NO: 95-248. In a more preferred embodiment, the nucleic acid molecule hybridizes under low, moderate or high stringency conditions to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule comprising a nucleic acid sequence selected from SEQ ID NO: 1-94.

Nucleic acid molecules of the present invention may also comprise nucleic acid sequences that exhibit substantial sequence similarity to a nucleic acid encoding a CSP or a complement of the encoding nucleic acid molecule. In this embodiment, it is preferred that the nucleic acid molecule exhibit substantial sequence similarity to a nucleic acid molecule encoding human CSP. More preferred is a nucleic acid molecule exhibiting substantial sequence similarity to a nucleic acid molecule encoding a polypeptide having an amino acid sequence of SEQ ID NO: 95-248. By substantial sequence similarity it is meant a nucleic acid molecule having at least 60%, more preferably at least 70%, even more preferably at least 80% and even more preferably at least 85% sequence identity with a nucleic acid molecule encoding a CSP, such as a polypeptide having an amino acid sequence of SEQ ID NO: 95-248. In a more preferred embodiment, the similar nucleic acid molecule is one that has at least 90%, more preferably at least 95%, more preferably at least 97%, even more preferably at least 98%, and still more preferably at least 99% sequence identity with a nucleic acid molecule encoding a CSP. Most preferred in this embodiment is a nucleic acid molecule that has at least 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity with a nucleic acid molecule encoding a CSP.

The nucleic acid molecules of the present invention are also inclusive of those exhibiting substantial sequence similarity to a CSNA or its complement. In this embodiment, it is preferred that the nucleic acid molecule exhibit substantial sequence similarity to a nucleic acid molecule having a nucleic acid sequence of SEQ ID NO: 1-94.

By substantial sequence similarity it is meant a nucleic acid molecule that has at least 60%, more preferably at least 70%, even more preferably at least 80% and even more preferably at least 85% sequence identity with a CSNA, such as one having a nucleic acid sequence of SEQ ID NO: 1-94. More preferred is a nucleic acid molecule that has at least 90%, more preferably at least 95%, more preferably at least 97%, even more preferably at least 98%, and still more preferably at least 99% sequence identity with a CSNA. Most preferred is a nucleic acid molecule that has at least 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity with a CSNA.

Nucleic acid molecules that exhibit substantial sequence similarity are inclusive of sequences that exhibit sequence identity over their entire length to a CSNA or to a nucleic acid molecule encoding a CSP, as well as sequences that are similar over only a part of its length. In this case, the part is at least 50 nucleotides of the CSNA or the nucleic acid molecule encoding a CSP, preferably at least 100 nucleotides, more preferably at least 150 or 200 nucleotides, even more preferably at least 250 or 300 nucleotides, still more preferably at least 400 or 500 nucleotides.

The substantially similar nucleic acid molecule may be a naturally occurring one that is derived from another species, especially one derived from another primate, wherein the similar nucleic acid molecule encodes an amino acid sequence that exhibits significant sequence identity to that of SEQ ID NO: 95-248 or demonstrates significant sequence identity to the nucleotide sequence of SEQ ID NO: 1-94. The similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule from a human, when the CSNA is a member of a gene family. The similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule derived from a non-primate, mammalian species, including without limitation, domesticated species, *e.g.*, dog, cat, mouse, rat, rabbit, hamster, cow, horse and pig; and wild animals, *e.g.*, monkey, fox, lions, tigers, bears, giraffes, zebras, etc. The substantially similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule derived from a non-mammalian species, such as birds or reptiles. The naturally occurring substantially similar nucleic acid molecule may be isolated directly from humans or other species. In another embodiment, the substantially similar nucleic acid molecule may be one that is experimentally produced by random mutation of a nucleic acid molecule. In another embodiment, the substantially similar nucleic acid molecule may be one that is experimentally produced by directed

mutation of a CSNA. In a preferred embodiment, the substantially similar nucleic acid molecule is a CSNA.

The nucleic acid molecules of the present invention are also inclusive of allelic variants of a CSNA or a nucleic acid encoding a CSP. For example, single nucleotide polymorphisms (SNPs) occur frequently in eukaryotic genomes and the sequence determined from one individual of a species may differ from other allelic forms present within the population. More than 1.4 million SNPs have already been identified in the human genome, International Human Genome Sequencing Consortium, *Nature* 409: 860-921 (2001) – Variants with small deletions and insertions of more than a single nucleotide are also found in the general population, and often do not alter the function of the protein. In addition, amino acid substitutions occur frequently among natural allelic variants, and often do not substantially change protein function.

In a preferred embodiment, the allelic variant is a variant of a gene, wherein the gene is transcribed into a mRNA that encodes a CSP. In a more preferred embodiment, the gene is transcribed into a mRNA that encodes a CSP comprising an amino acid sequence of SEQ ID NO: 95-248. In another preferred embodiment, the allelic variant is a variant of a gene, wherein the gene is transcribed into a mRNA that is a CSNA. In a more preferred embodiment, the gene is transcribed into a mRNA that comprises the nucleic acid sequence of SEQ ID NO: 1-94. Also preferred is that the allelic variant be a naturally occurring allelic variant in the species of interest, particularly human.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences comprising a part of a nucleic acid sequence of the instant invention. The part may or may not encode a polypeptide, and may or may not encode a polypeptide that is a CSP. In a preferred embodiment, the part encodes a CSP. In one embodiment, the nucleic acid molecule comprises a part of a CSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that hybridizes or exhibits substantial sequence similarity to a CSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that is an allelic variant of a CSNA. In yet another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that encodes a CSP. A part comprises at least 10 nucleotides, more preferably at least 15, 17, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400 or 500 nucleotides. The maximum size of a nucleic acid part is one nucleotide shorter than the sequence of the nucleic acid molecule encoding the full-length protein.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences that encode fusion proteins, homologous proteins, polypeptide fragments, muteins and polypeptide analogs, as described *infra*.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences containing modifications of the native nucleic acid molecule. Examples of such modifications include, but are not limited to, nonnative internucleoside bonds, post-synthetic modifications or altered nucleotide analogues. One having ordinary skill in the art would recognize that the type of modification that may be made will depend upon the intended use of the nucleic acid molecule. For instance, when the nucleic acid molecule is used as a hybridization probe, the range of such modifications will be limited to those that permit sequence-discriminating base pairing of the resulting nucleic acid. When used to direct expression of RNA or protein *in vitro* or *in vivo*, the range of such modifications will be limited to those that permit the nucleic acid to function properly as a polymerization substrate. When the isolated nucleic acid is used as a therapeutic agent, the modifications will be limited to those that do not confer toxicity upon the isolated nucleic acid.

Accordingly, in one embodiment, a nucleic acid molecule may include nucleotide analogues that incorporate labels that are directly detectable, such as radiolabels or fluorophores, or nucleotide analogues that incorporate labels that can be visualized in a subsequent reaction, such as biotin or various haptens. The labeled nucleic acid molecules are particularly useful as hybridization probes.

Common radiolabeled analogues include those labeled with ^{33}P , ^{32}P , and ^{35}S , such as α - ^{32}P -dATP, α - ^{32}P -dCTP, α - ^{32}P -dGTP, α - ^{32}P -dTTP, α - ^{32}P -3'dATP, α - ^{32}P -ATP, α - ^{32}P -CTP, α - ^{32}P -GTP, α - ^{32}P -UTP, α - ^{35}S -dATP, γ - ^{35}S -GTP, γ - ^{33}P -dATP, and the like.

Commercially available fluorescent nucleotide analogues readily incorporated into the nucleic acids of the present invention include Cy3-dCTP, Cy3-dUTP, Cy5-dCTP, Cy3-dUTP (Amersham Biosciences, Piscataway, New Jersey, USA), fluorescein-12-dUTP, tetramethylrhodamine-6-dUTP, Texas Red®-5-dUTP, Cascade Blue®-7-dUTP, BODIPY® FL-14-dUTP, BODIPY® TMR-14-dUTP, BODIPY® TR-14-dUTP, Rhodamine Green™-5-dUTP, Oregon Green® 488-5-dUTP, Texas Red®-12-dUTP, BODIPY® 630/650-14-dUTP, BODIPY® 650/665-14-dUTP, Alexa Fluor® 488-5-dUTP, Alexa Fluor® 532-5-dUTP, Alexa Fluor® 568-5-dUTP, Alexa Fluor® 594-5-dUTP, Alexa Fluor® 546-14-dUTP, fluorescein-12-UTP, tetramethylrhodamine-6-UTP, Texas

Red®-5-UTP, Cascade Blue®-7-UTP, BODIPY® FL-14-UTP, BODIPY® TMR-14-UTP, BODIPY® TR-14-UTP, Rhodamine Green™-5-UTP, Alexa Fluor® 488-5-UTP, Alexa Fluor® 546-14-UTP (Molecular Probes, Inc. Eugene, OR, USA). One may also custom synthesize nucleotides having other fluorophores. See Henegariu *et al.*, *Nature*

5 *Biotechnol.* 18: 345-348 (2000).

Haptens that are commonly conjugated to nucleotides for subsequent labeling include biotin (biotin-11-dUTP, Molecular Probes, Inc., Eugene, OR, USA; biotin-21-UTP, biotin-21-dUTP, Clontech Laboratories, Inc., Palo Alto, CA, USA), digoxigenin (DIG-11-dUTP, alkali labile, DIG-11-UTP, Roche Diagnostics Corp., Indianapolis, IN, USA), and dinitrophenyl (dinitrophenyl-11-dUTP, Molecular Probes, Inc., Eugene, OR, USA).

Nucleic acid molecules of the present invention can be labeled by incorporation of labeled nucleotide analogues into the nucleic acid. Such analogues can be incorporated by enzymatic polymerization, such as by nick translation, random priming, polymerase chain reaction (PCR), terminal transferase tailing, and end-filling of overhangs, for DNA molecules, and *in vitro* transcription driven, *e.g.*, from phage promoters, such as T7, T3, and SP6, for RNA molecules. Commercial kits are readily available for each such labeling approach. Analogues can also be incorporated during automated solid phase chemical synthesis. Labels can also be incorporated after nucleic acid synthesis, with the 5' phosphate and 3' hydroxyl providing convenient sites for post-synthetic covalent attachment of detectable labels.

Other post-synthetic approaches also permit internal labeling of nucleic acids. For example, fluorophores can be attached using a cisplatin reagent that reacts with the N7 of guanine residues (and, to a lesser extent, adenine bases) in DNA, RNA, and Peptide Nucleic Acids (PNA) to provide a stable coordination complex between the nucleic acid and fluorophore label (Universal Linkage System) (available from Molecular Probes, Inc., Eugene, OR, USA and Amersham Pharmacia Biotech, Piscataway, NJ, USA); see Alers *et al.*, *Genes, Chromosomes & Cancer* 25: 301-305 (1999); Jelsma *et al.*, *J. NIH Res.* 5: 82 (1994); Van Belkum *et al.*, *BioTechniques* 16: 148-153 (1994). Alternatively, nucleic acids can be labeled using a disulfide-containing linker (FastTag™ Reagent, Vector Laboratories, Inc., Burlingame, CA, USA) that is photo- or thermally coupled to the target nucleic acid using aryl azide chemistry; after reduction, a free thiol is available for coupling to a hapten, fluorophore, sugar, affinity ligand, or other marker.

One or more independent or interacting labels can be incorporated into the nucleic acid molecules of the present invention. For example, both a fluorophore and a moiety that in proximity thereto acts to quench fluorescence can be included to report specific hybridization through release of fluorescence quenching or to report exonucleotidic excision. See, e.g., Tyagi *et al.*, *Nature Biotechnol.* 14: 303-308 (1996); Tyagi *et al.*, *Nature Biotechnol.* 16: 49-53 (1998); Sokol *et al.*, *Proc. Natl. Acad. Sci. USA* 95: 11538-11543 (1998); Kostrikis *et al.*, *Science* 279: 1228-1229 (1998); Marras *et al.*, *Genet. Anal.* 14: 151-156 (1999); Holland *et al.*, *Proc. Natl. Acad. Sci. USA* 88: 7276-7280 (1991); Heid *et al.*, *Genome Res.* 6(10): 986-94 (1996); Kuimelis *et al.*, *Nucleic Acids Symp. Ser.* (37): 255-6 (1997); and U.S. Patent Nos. 5,846,726, 5,925,517, 5,925,517, 5,723,591 and 5,538,848, the disclosures of which are incorporated herein by reference in their entirety.

Nucleic acid molecules of the present invention may also be modified by altering one or more native phosphodiester internucleoside bonds to more nuclease-resistant, internucleoside bonds. See Hartmann *et al.* (eds.), Manual of Antisense Methodology: Perspectives in Antisense Science, Kluwer Law International (1999); Stein *et al.* (eds.), Applied Antisense Oligonucleotide Technology, Wiley-Liss (1998); Chadwick *et al.* (eds.), Oligonucleotides as Therapeutic Agents – Symposium No. 209, John Wiley & Son Ltd (1997). Such altered internucleoside bonds are often desired for techniques or for targeted gene correction, Gamper *et al.*, *Nucl. Acids Res.* 28(21): 4332-4339 (2000). For double-stranded RNA inhibition which may utilize either natural ds RNA or ds RNA modified in its, sugar, phosphate or base, see Hannon, *Nature* 418(11): 244-251 (2002); Fire *et al.* in WO 99/32619; Tuschl *et al.* in US2002/0086356; Kruetzer *et al.* in WO 00/44895, the disclosures of which are incorporated herein by reference in their entirety. For circular antisense, see Kool in U.S. Patent No. 5,426,180, the disclosure of which is incorporated herein by reference in its entirety.

Modified oligonucleotide backbones include, without limitation, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotriesters, methyl and other alkyl phosphonates including 3'-alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates including 3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having normal 3'-5' linkages, 2'-5' linked analogs of these, and those having inverted polarity

wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5' to 5'-2'.

Representative U.S. Patents that teach the preparation of the above phosphorus-containing linkages include, but are not limited to, U.S. Patent Nos. 3,687,808; 4,469,863; 4,476,301; 5,023,243; 5,177,196; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,939; 5,453,496; 5,455,233; 5,466,677; 5,476,925; 5,519,126; 5,536,821; 5,541,306; 5,550,111; 5,563,253; 5,571,799; 5,587,361; and 5,625,050, the disclosures of which are incorporated herein by reference in their entireties. In a preferred embodiment, the modified internucleoside linkages may be used for antisense techniques.

Other modified oligonucleotide backbones do not include a phosphorus atom, but have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH₂ component parts. Representative U.S. patents that teach the preparation of the above backbones include, but are not limited to, U.S. Patent Nos. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437 and 5,677,439; the disclosures of which are incorporated herein by reference in their entireties.

In other preferred nucleic acid molecules, both the sugar and the internucleoside linkage are replaced with novel groups, such as peptide nucleic acids (PNA). In PNA compounds, the phosphodiester backbone of the nucleic acid is replaced with an amide-containing backbone, in particular by repeating N-(2-aminoethyl) glycine units linked by amide bonds. Nucleobases are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone, typically by methylene carbonyl linkages. PNA can be synthesized using a modified peptide synthesis protocol. PNA oligomers can be synthesized by both Fmoc and tBoc methods. Representative U.S. patents that teach the preparation of PNA compounds include, but are not limited to, U.S. Patent Nos.

5,539,082; 5,714,331; and 5,719,262, each of which is herein incorporated by reference in its entirety. Automated PNA synthesis is readily achievable on commercial synthesizers (see, e.g., "PNA User's Guide," Rev. 2, February 1998, Perseptive Biosystems Part No. 60138, Applied Biosystems, Inc., Foster City, CA). PNA molecules are advantageous for a number of reasons. First, because the PNA backbone is uncharged, PNA/DNA and PNA/RNA duplexes have a higher thermal stability than is found in DNA/DNA and DNA/RNA duplexes. The T_m of a PNA/DNA or PNA/RNA duplex is generally 1°C higher per base pair than the T_m of the corresponding DNA/DNA or DNA/RNA duplex (in 100 mM NaCl). Second, PNA molecules can also form stable PNA/DNA complexes at low ionic strength, under conditions in which DNA/DNA duplex formation does not occur. Third, PNA also demonstrates greater specificity in binding to complementary DNA because a PNA/DNA mismatch is more destabilizing than DNA/DNA mismatch. A single mismatch in mixed a PNA/DNA 15-mer lowers the T_m by 8–20°C (15°C on average). In the corresponding DNA/DNA duplexes, a single mismatch lowers the T_m by 4–16°C (11°C on average). Because PNA probes can be significantly shorter than DNA probes, their specificity is greater. Fourth, PNA oligomers are resistant to degradation by enzymes, and the lifetime of these compounds is extended both *in vivo* and *in vitro* because nucleases and proteases do not recognize the PNA polyamide backbone with nucleobase sidechains. See, e.g., Ray *et al.*, *FASEB J.* 14(9): 1041-60 (2000); Nielsen *et al.*, *Pharmacol Toxicol.* 86(1): 3-7 (2000); Larsen *et al.*, *Biochim Biophys Acta.* 1489(1): 159-66 (1999); Nielsen, *Curr. Opin. Struct. Biol.* 9(3): 353-7 (1999), and Nielsen, *Curr. Opin. Biotechnol.* 10(1): 71-5 (1999).

Nucleic acid molecules may be modified compared to their native structure throughout the length of the nucleic acid molecule or can be localized to discrete portions thereof. As an example of the latter, chimeric nucleic acids can be synthesized that have discrete DNA and RNA domains and that can be used for targeted gene repair and modified PCR reactions, as further described in, Misra *et al.*, *Biochem.* 37: 1917-1925 (1998); and Finn *et al.*, *Nucl. Acids Res.* 24: 3357-3363 (1996), and U.S. Patent Nos. 5,760,012 and 5,731,181, the disclosures of which are incorporated herein by reference in their entireties.

Unless otherwise specified, nucleic acid molecules of the present invention can include any topological conformation appropriate to the desired use; the term thus explicitly comprehends, among others, single-stranded, double-stranded, triplexed,

quadruplexed, partially double-stranded, partially-triplexed, partially-quadruplexed, branched, hairpinned, circular, and padlocked conformations. Padlocked conformations and their utilities are further described in Banér *et al.*, *Curr. Opin. Biotechnol.* 12: 11-15 (2001); Escude *et al.*, *Proc. Natl. Acad. Sci. USA* 14: 96(19):10603-7 (1999); and Nilsson
5 *et al.*, *Science* 265(5181): 2085-8 (1994). Triplexed and quadruplexed conformations, and their utilities, are reviewed in Praseuth *et al.*, *Biochim. Biophys. Acta.* 1489(1): 181-206 (1999); Fox, *Curr. Med. Chem.* 7(1): 17-37 (2000); Kochetkova *et al.*, *Methods Mol. Biol.* 130: 189-201 (2000); Chan *et al.*, *J. Mol. Med.* 75(4): 267-82 (1997); Rowley *et al.*, *Mol Med* 5(10): 693-700 (1999); Kool, *Annu Rev Biophys Biomol Struct.* 25: 1-28 (1996).

10 *SNP Polymorphisms*

Commonly, sequence differences between individuals involve differences in single nucleotide positions. SNPs may account for 90% of human DNA polymorphism. Collins
et al., 8 *Genome Res.* 1229-31 (1998). SNPs include single base pair positions in genomic DNA at which different sequence alternatives (alleles) exist in a population. In addition,
15 the least frequent allele generally must occur at a frequency of 1% or greater. DNA sequence variants with a reasonably high population frequency are observed approximately every 1,000 nucleotide across the genome, with estimates as high as 1 SNP per 350 base pairs. Wang *et al.*, 280 *Science* 1077-82 (1998); Harding *et al.*, 60 *Am. J. Human Genet.* 772-89 (1997); Taillon-Miller *et al.*, 8 *Genome Res.* 748-54 (1998); Cargill
20 *et al.*, 22 *Nat. Genet.* 231-38 (1999); and Semple *et al.*, 16 *Bioinform. Disc. Note* 735-38 (2000). The frequency of SNPs varies with the type and location of the change. In base substitutions, two-thirds of the substitutions involve the C-T and G-A type. This variation in frequency can be related to 5-methylcytosine deamination reactions that occur frequently, particularly at CpG dinucleotides. Regarding location, SNPs occur at a much
25 higher frequency in non-coding regions than in coding regions. Information on over one million variable sequences is already publicly available via the Internet and more such markers are available from commercial providers of genetic information. Kwok and Gu, 5 *Med. Today* 538-53 (1999).

Several definitions of SNPs exist. See, e.g., Brooks, 235 *Gene* 177-86 (1999). As
30 used herein, the term "single nucleotide polymorphism" or "SNP" includes all single base variants, thus including nucleotide insertions and deletions in addition to single nucleotide substitutions. There are two types of nucleotide substitutions. A transition is the

replacement of one purine by another purine or one pyrimidine by another pyrimidine. A transversion is the replacement of a purine for a pyrimidine, or vice versa.

Numerous methods exist for detecting SNPs within a nucleotide sequence. A review of many of these methods can be found in Landegren *et al.*, 8 *Genome Res.* 769-76
5 (1998). For example, a SNP in a genomic sample can be detected by preparing a Reduced Complexity Genome (RCG) from the genomic sample, then analyzing the RCG for the presence or absence of a SNP. See, e.g., WO 00/18960 which is herein incorporated by reference in its entirety. Multiple SNPs in a population of target polynucleotides in parallel can be detected using, for example, the methods of WO 00/50869 which is herein
10 incorporated by reference in its entirety. Other SNP detection methods include the methods of U.S. Pat. Nos. 6,297,018 and 6,322,980 which are herein incorporated by reference in their entirety. Furthermore, SNPs can be detected by restriction fragment length polymorphism (RFLP) analysis. See, e.g., U.S. Pat. Nos. 5,324,631; 5,645,995 which are herein incorporated by reference in their entirety. RFLP analysis of SNPs,
15 however, is limited to cases where the SNP either creates or destroys a restriction enzyme cleavage site. SNPs can also be detected by direct sequencing of the nucleotide sequence of interest. In addition, numerous assays based on hybridization have also been developed to detect SNPs and mismatch distinction by polymerases and ligases. Several web sites provide information about SNPs including Ensembl on the World Wide Web at
20 ensemble.org, Sanger Institute on the World Wide Web at sanger.ac.uk/genetics/exon/, National Center for Biotechnology Information (NCBI) on the World Wide Web at ncbi.nlm.nih.gov/SNP/, The SNP Consortium Ltd. on the World Wide Web at snp.cshl.org. The chromosomal locations for the compositions disclosed herein are provided below. In addition, one of ordinary skill in the art could use a BLAST against
25 the genome or any of the databases cited above to find the chromosomal location. Another a preferred method to find the genomic coordinates and associated SNPs would be to use the BLAT tool (genome.ucsc.edu, Kent et al. 2001, The Human Genome Browser at UCSC, Genome Research 996-1006 or Kent 2002 BLAT —The BLAST -Like Alignment Tool Genome Reseach, 1-9). All web sites above were accessed December 3,
30 2003.

RNA interference refers to the process of sequence-specific post transcriptional gene silencing in animals mediated by short interfering RNAs (siRNA). Fire *et al.*, 1998, *Nature*, 391, 806. The corresponding process in plants is commonly referred to as post transcriptional gene silencing or RNA silencing and is also referred to as quelling in fungi.

- 5 The process of post transcriptional gene silencing is thought to be an evolutionarily conserved cellular defense mechanism used to prevent the expression of foreign genes which is commonly shared by diverse flora and phyla. Fire *et al.*, 1999, *Trends Genet.*, 15, 358. Such protection from foreign gene expression may have evolved in response to the production of double-stranded RNAs (dsRNA) derived from viral infection or the
- 10 random integration of transposon elements into a host genome via a cellular response that specifically destroys homologous single-stranded RNA or viral genomic RNA. The presence of dsRNA in cells triggers the RNAi response through a mechanism that has yet to be fully characterized. This mechanism appears to be different from the interferon response that results from dsRNA mediated activation of protein kinase PKR and 2',5'-
- 15 oligoadenylate synthetase resulting in non-specific cleavage of mRNA by ribonuclease L.

- The presence of long dsRNAs in cells stimulates the activity of a ribonuclease III enzyme referred to as dicer. Dicer is involved in the processing of the dsRNA into short pieces of dsRNA known as short interfering RNAs (siRNA). Berstein *et al.*, 2001, *Nature*, 409, 363. Short interfering RNAs derived from dicer activity are typically about
- 20 21-23 nucleotides in length and comprise about 19 base pair duplexes. Dicer has also been implicated in the excision of 21 and 22 nucleotide small temporal RNAs (stRNA) from precursor RNA of conserved structure that are implicated in translational control. Hutvagner *et al.*, 2001, *Science*, 293, 834. The RNAi response also features an endonuclease complex containing a siRNA, commonly referred to as an RNA-induced
- 25 silencing complex (RISC), which mediates cleavage of single stranded RNA having sequence complementary to the antisense strand of the siRNA duplex. Cleavage of the target RNA takes place in the middle of the region complementary to the antisense strand of the siRNA duplex. Elbashir *et al.*, 2001, *Genes Dev.*, 15, 188.

- Short interfering RNA mediated RNAi has been studied in a variety of systems.
- 30 Fire *et al.*, 1998, *Nature*, 391, 806, were the first to observe RNAi in *C. Elegans*. Wianny and Goetz, 1999, *Nature Cell Biol.*, 2, 70, describe RNAi mediated by dsRNA in mouse embryos. Hammond *et al.*, 2000, *Nature*, 404, 293, describe RNAi in *Drosophila* cells

transfected with dsRNA. Elbashir *et al.*, 2001, *Nature*, 411, 494, describe RNAi induced by introduction of duplexes of synthetic 21-nucleotide RNAs in cultured mammalian cells including human embryonic kidney and HeLa cells. Recent work in *Drosophila* embryonic lysates (Elbashir *et al.*, 2001, *EMBO J.*, 20, 6877) has revealed certain requirements for
5 siRNA length, structure, chemical composition, and sequence that are essential to mediate efficient RNAi activity. These studies have shown that 21 nucleotide siRNA duplexes are most active when containing two nucleotide 3'-overhangs. Furthermore, complete substitution of one or both siRNA strands with 2'-deoxy (2'-H) or 2'-O-methyl nucleotides abolishes RNAi activity, whereas substitution of the 3'-terminal siRNA overhang
10 nucleotides with deoxy nucleotides (2'-H) was shown to be tolerated. Single mismatch sequences in the center of the siRNA duplex were also shown to abolish RNAi activity. In addition, these studies also indicate that the position of the cleavage site in the target RNA is defined by the 5'-end of the siRNA guide sequence rather than the 3'-end. Elbashir *et al.*, 2001, *EMBO J.*, 20, 6877. Other studies have indicated that a 5'-phosphate on the
15 target-complementary strand of a siRNA duplex is required for siRNA activity and that ATP is utilized to maintain the 5'-phosphate moiety on the siRNA. Nykanen *et al.*, 2001, *Cell*, 107, 309.

Studies have shown that replacing the 3'-overhanging segments of a 21-mer siRNA duplex having 2 nucleotide 3' overhangs with deoxyribonucleotides does not have an
20 adverse effect on RNAi activity. Replacing up to 4 nucleotides on each end of the siRNA with deoxyribonucleotides has been reported to be well tolerated whereas complete substitution with deoxyribonucleotides results in no RNAi activity. Elbashir *et al.*, 2001, *EMBO J.*, 20, 6877. In addition, Elbashir *et al.*, *supra*, also report that substitution of siRNA with 2'-O-methyl nucleotides completely abolishes RNAi activity. Li *et al.*, WO
25 00/44914, and Beach *et al.*, WO 01/68836 both suggest that siRNA "may include modifications to either the phosphate-sugar back bone or the nucleoside to include at least one of a nitrogen or sulfur heteroatom", however neither application teaches to what extent these modifications are tolerated in siRNA molecules nor provide any examples of such modified siRNA. Kreutzer and Limmer, Canadian Patent Application No. 2,359,180, also
30 describe certain chemical modifications for use in dsRNA constructs in order to counteract activation of double stranded RNA-dependent protein kinase PKR, specifically 2'-amino or 2'-O-methyl nucleotides, and nucleotides containing a 2'-O or 4'-C methylene bridge. However, Kreutzer and Limmer similarly fail to show to what extent these modifications

are tolerated in siRNA molecules nor do they provide any examples of such modified siRNA.

Parrish et al., 2000, *Molecular Cell*, 6, 1977-1087, tested certain chemical modifications targeting the unc-22 gene in *C. elegans* using long (>25 nt) siRNA transcripts. The authors describe the introduction of thiophosphate residues into these
5 siRNA transcripts by incorporating thiophosphate nucleotide analogs with T7 and T3 RNA polymerase and observed that "RNAs with two [phosphorothioate] modified bases also had substantial decreases in effectiveness as RNAi triggers; [phosphorothioate] modification of more than two residues greatly destabilized the RNAs in vitro and we
10 were not able to assay interference activities." Parrish et al. at 1081. The authors also tested certain modifications at the 2'-position of the nucleotide sugar in the long siRNA transcripts and observed that substituting deoxynucleotides for ribonucleotides "produced a substantial decrease in interference activity", especially in the case of Uridine to Thymidine and/or Cytidine to deoxy-Cytidine substitutions. Parrish et al. In addition, the
15 authors tested certain base modifications, including substituting 4-thiouracil, 5-bromouracil, 5-iodouracil, 3-(aminoallyl)uracil for uracil, and inosine for guanosine in sense and antisense strands of the siRNA, and found that whereas 4-thiouracil and 5-bromouracil were all well tolerated, inosine "produced a substantial decrease in interference activity" when incorporated in either strand. Incorporation of 5-iodouracil and
20 3-(aminoallyl)uracil in the antisense strand resulted in substantial decrease in RNAi activity as well.

Beach et al., WO 01/68836, describes specific methods for attenuating gene expression using endogenously derived dsRNA. Tuschl et al., WO 01/75164, describes a
25 *Drosophila* in vitro RNAi system and the use of specific siRNA molecules for certain functional genomic and certain therapeutic applications; although Tuschl, 2001, *Chem. Biochem.*, 2, 239-245, doubts that RNAi can be used to cure genetic diseases or viral infection due "to the danger of activating interferon response". Li et al., WO 00/44914, describes the use of specific dsRNAs for use in attenuating the expression of certain target genes. Zernicka-Goetz et al., WO 01/36646, describes certain methods for inhibiting the
30 expression of particular genes in mammalian cells using certain dsRNA molecules. Fire et al., WO 99/32619, U.S. Patent No. 6,506,559, the contents of which are hereby incorporated by reference in their entirety, describes particular methods for introducing

certain dsRNA molecules into cells for use in inhibiting gene expression. Plaetinck et al., WO 00/01846, describes certain methods for identifying specific genes responsible for conferring a particular phenotype in a cell using specific dsRNA molecules. Mello et al., WO 01/29058, describes the identification of specific genes involved in dsRNA mediated RNAi. Deschamps Depaillette et al., International PCT Publication No. WO 99/07409, describes specific compositions consisting of particular dsRNA molecules combined with certain anti-viral agents. Driscoll et al., International PCT Publication No. WO 01/49844, describes specific DNA constructs for use in facilitating gene silencing in targeted organisms. Parrish et al., 2000, Molecular Cell, 6, 1977-1087, describes specific chemically modified siRNA constructs targeting the unc-22 gene of *C. elegans*. Tuschl et al., International PCT Publication No. WO 02/44321, describe certain synthetic siRNA constructs.

Methods for Using Nucleic Acid Molecules as Probes and Primers

The isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize, and quantify hybridizing nucleic acids in, and isolate hybridizing nucleic acids from, both genomic and transcript-derived nucleic acid samples. When free in solution, such probes are typically, but not invariably, detectably labeled; bound to a substrate, as in a microarray, such probes are typically, but not invariably unlabeled.

In one embodiment, the isolated nucleic acid molecules of the present invention can be used as probes to detect and characterize gross alterations in the gene of a CSNA, such as deletions, insertions, translocations, and duplications of the CSNA genomic locus through fluorescence *in situ* hybridization (FISH) to chromosome spreads. See, e.g., Andreeff et al. (eds.), Introduction to Fluorescence In Situ Hybridization: Principles and Clinical Applications, John Wiley & Sons (1999). The isolated nucleic acid molecules of the present invention can be used as probes to assess smaller genomic alterations using, e.g., Southern blot detection of restriction fragment length polymorphisms. The isolated nucleic acid molecules of the present invention can be used as probes to isolate genomic clones that include a nucleic acid molecule of the present invention, which thereafter can be restriction mapped and sequenced to identify deletions, insertions, translocations, and substitutions (single nucleotide polymorphisms, SNPs) at the sequence level.

Alternatively, detection techniques such as molecular beacons may be used, see Kostrikis *et al. Science* 279:1228-1229 (1998).

The isolated nucleic acid molecules of the present invention can also be used as probes to detect, characterize, and quantify CSNA in, and isolate CSNA from, transcript-derived nucleic acid samples. In one embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize by length, and quantify mRNA by Northern blot of total or poly-A⁺-selected RNA samples. In another embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize by location, and quantify mRNA by *in situ* hybridization to tissue sections. See, e.g., Schwarchzacher *et al.*, In Situ Hybridization, Springer-Verlag New York (2000). In another preferred embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to measure the representation of clones in a cDNA library or to isolate hybridizing nucleic acid molecules acids from cDNA libraries, permitting sequence level characterization of mRNAs that hybridize to CSNAs, including, without limitations, identification of deletions, insertions, substitutions, truncations, alternatively spliced forms and single nucleotide polymorphisms. In yet another preferred embodiment, the nucleic acid molecules of the instant invention may be used in microarrays.

All of the aforementioned probe techniques are well within the skill in the art, and are described at greater length in standard texts such as Sambrook (2001), *supra*; Ausubel (1999), *supra*; and Walker *et al.* (eds.), The Nucleic Acids Protocols Handbook, Humana Press (2000).

In another embodiment, a nucleic acid molecule of the invention may be used as a probe or primer to identify and/or amplify a second nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of the invention. In this embodiment, it is preferred that the probe or primer be derived from a nucleic acid molecule encoding a CSP. More preferably, the probe or primer is derived from a nucleic acid molecule encoding a polypeptide having an amino acid sequence of SEQ ID NO: 95-248. Also preferred are probes or primers derived from a CSNA. More preferred are probes or primers derived from a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-94.

In general, a probe or primer is at least 10 nucleotides in length, more preferably at least 12, more preferably at least 14 and even more preferably at least 16 or 17 nucleotides

in length. In an even more preferred embodiment, the probe or primer is at least 18 nucleotides in length, even more preferably at least 20 nucleotides and even more preferably at least 22 nucleotides in length. Primers and probes may also be longer in length. For instance, a probe or primer may be 25 nucleotides in length, or may be 30, 40
5 or 50 nucleotides in length. Methods of performing nucleic acid hybridization using oligonucleotide probes are well known in the art. *See, e.g.*, Sambrook *et al.*, 1989, *supra*, Chapter 11 and pp. 11.31-11.32 and 11.40-11.44, which describes radiolabeling of short probes, and pp. 11.45-11.53, which describe hybridization conditions for oligonucleotide probes, including specific conditions for probe hybridization (pp. 11.50-11.51).

10 Methods of performing primer-directed amplification are also well known in the art. Methods for performing the polymerase chain reaction (PCR) are compiled, *inter alia*, in McPherson, PCR Basics: From Background to Bench, Springer Verlag (2000); Innis *et al.* (eds.), PCR Applications: Protocols for Functional Genomics, Academic Press (1999); Gelfand *et al.* (eds.), PCR Strategies, Academic Press (1998); Newton *et al.*, PCR,
15 Springer-Verlag New York (1997); Burke (ed.), PCR: Essential Techniques, John Wiley & Son Ltd (1996); White (ed.), PCR Cloning Protocols: From Molecular Cloning to Genetic Engineering, Vol. 67, Humana Press (1996); and McPherson *et al.* (eds.), PCR 2: A Practical Approach, Oxford University Press, Inc. (1995). Methods for performing RT-PCR are collected, *e.g.*, in Siebert *et al.* (eds.), Gene Cloning and Analysis by RT-PCR,
20 Eaton Publishing Company/Bio Techniques Books Division, 1998; and Siebert (ed.), PCR Technique: RT-PCR, Eaton Publishing Company/ BioTechniques Books (1995).

PCR and hybridization methods may be used to identify and/or isolate nucleic acid molecules of the present invention including allelic variants, homologous nucleic acid molecules and fragments. PCR and hybridization methods may also be used to identify,
25 amplify and/or isolate nucleic acid molecules of the present invention that encode homologous proteins, analogs, fusion protein or muteins of the invention. Nucleic acid primers as described herein can be used to prime amplification of nucleic acid molecules of the invention, using transcript-derived or genomic DNA as the template.

These nucleic acid primers can also be used, for example, to prime single base
30 extension (SBE) for SNP detection (*See, e.g.*, U.S. Pat. No. 6,004,744, the disclosure of which is incorporated herein by reference in its entirety).

Isothermal amplification approaches, such as rolling circle amplification, are also now well-described. *See, e.g.*, Schweitzer *et al.*, *Curr. Opin. Biotechnol.* 12(1): 21-7

(2001); International Patent publications WO 97/19193 and WO 00/15779, and U.S. Patent Nos. 5,854,033 and 5,714,320, the disclosures of which are incorporated herein by reference in their entireties. Rolling circle amplification can be combined with other techniques to facilitate SNP detection. See, e.g., Lizardi *et al.*, *Nature Genet.* 19(3):
5 225-32 (1998).

Nucleic acid molecules of the present invention may be bound to a substrate either covalently or noncovalently. The substrate can be porous or solid, planar or non-planar, unitary or distributed. The bound nucleic acid molecules may be used as hybridization probes, and may be labeled or unlabeled. In a preferred embodiment, the bound nucleic
10 acid molecules are unlabeled.

In one embodiment, the nucleic acid molecule of the present invention is bound to a porous substrate, e.g., a membrane, typically comprising nitrocellulose, nylon, or positively charged derivatized nylon. The nucleic acid molecule of the present invention can be used to detect a hybridizing nucleic acid molecule that is present within a labeled
15 nucleic acid sample, e.g., a sample of transcript-derived nucleic acids. In another embodiment, the nucleic acid molecule is bound to a solid substrate, including, without limitation, glass, amorphous silicon, crystalline silicon or plastics. Examples of plastics include, without limitation, polymethylacrylic, polyethylene, polypropylene, polyacrylate, polymethylmethacrylate, polyvinylchloride, polytetrafluoroethylene, polystyrene,
20 polycarbonate, polyacetal, polysulfone, celluloseacetate, cellulosenitrate, nitrocellulose, or mixtures thereof. The solid substrate may be any shape, including rectangular, disk-like and spherical. In a preferred embodiment, the solid substrate is a microscope slide or slide-shaped substrate.

The nucleic acid molecule of the present invention can be attached covalently to a
25 surface of the support substrate or applied to a derivatized surface in a chaotropic agent that facilitates denaturation and adherence by presumed noncovalent interactions, or some combination thereof. The nucleic acid molecule of the present invention can be bound to a substrate to which a plurality of other nucleic acids are concurrently bound, hybridization to each of the plurality of bound nucleic acids being separately detectable. At low density,
30 e.g. on a porous membrane, these substrate-bound collections are typically denominated macroarrays; at higher density, typically on a solid support, such as glass, these substrate bound collections of plural nucleic acids are colloquially termed microarrays. As used herein, the term microarray includes arrays of all densities. It is, therefore, another aspect

of the invention to provide microarrays that comprise one or more of the nucleic acid molecules of the present invention.

In yet another embodiment, the invention is directed to single exon probes based on the CSNAs disclosed herein.

5 *Expression Vectors, Host Cells and Recombinant Methods of Producing Polypeptides*

Another aspect of the present invention provides vectors that comprise one or more of the isolated nucleic acid molecules of the present invention, and host cells in which such vectors have been introduced.

10 The vectors can be used, *inter alia*, for propagating the nucleic acid molecules of the present invention in host cells (cloning vectors), for shuttling the nucleic acid molecules of the present invention between host cells derived from disparate organisms (shuttle vectors), for inserting the nucleic acid molecules of the present invention into host cell chromosomes (insertion vectors), for expressing sense or antisense RNA transcripts of
15 the nucleic acid molecules of the present invention *in vitro* or within a host cell, and for expressing polypeptides encoded by the nucleic acid molecules of the present invention, alone or as fusion proteins with heterologous polypeptides (expression vectors). Vectors are by now well known in the art, and are described, *inter alia*, in Jones *et al.* (eds.), Vectors: Cloning Applications: Essential Techniques (Essential Techniques Series), John
20 Wiley & Son Ltd. (1998); Jones *et al.* (eds.), Vectors: Expression Systems: Essential Techniques (Essential Techniques Series), John Wiley & Son Ltd. (1998); Gacesa *et al.*, Vectors: Essential Data, John Wiley & Sons Ltd. (1995); Cid-Arregui (eds.), Viral Vectors: Basic Science and Gene Therapy, Eaton Publishing Co. (2000); Sambrook (2001), *supra*; Ausubel (1999), *supra*. Furthermore, a variety of vectors are available
25 commercially. Use of existing vectors and modifications thereof are well within the skill in the art. Thus, only basic features need be described here.

Nucleic acid sequences may be expressed by operatively linking them to an expression control sequence in an appropriate expression vector and employing that expression vector to transform an appropriate unicellular host. Expression control
30 sequences are sequences that control the transcription, post-transcriptional events and translation of nucleic acid sequences. Such operative linking of a nucleic acid sequence of this invention to an expression control sequence, of course, includes, if not already part of

the nucleic acid sequence, the provision of a translation initiation codon, ATG or GTG, in the correct reading frame upstream of the nucleic acid sequence.

A wide variety of host/expression vector combinations may be employed in expressing the nucleic acid sequences of this invention. Useful expression vectors, for example, may consist of segments of chromosomal, non-chromosomal and synthetic nucleic acid sequences.

In one embodiment, prokaryotic cells may be used with an appropriate vector. Prokaryotic host cells are often used for cloning and expression. In a preferred embodiment, prokaryotic host cells include *E. coli*, *Pseudomonas*, *Bacillus* and *Streptomyces*. In a preferred embodiment, bacterial host cells are used to express the nucleic acid molecules of the instant invention. Useful expression vectors for bacterial hosts include bacterial plasmids, such as those from *E. coli*, *Bacillus* or *Streptomyces*, including pBluescript, pGEX-2T, pUC vectors, col E1, pCR1, pBR322, pMB9 and their derivatives, wider host range plasmids, such as RP4, phage DNAs, *e.g.*, the numerous derivatives of phage lambda, *e.g.*, NM989, λ GT10 and λ GT11, and other phages, *e.g.*, M13 and filamentous single stranded phage DNA. Where *E. coli* is used as host, selectable markers are, analogously, chosen for selectivity in gram negative bacteria: *e.g.*, typical markers confer resistance to antibiotics, such as ampicillin, tetracycline, chloramphenicol, kanamycin, streptomycin and zeocin; auxotrophic markers can also be used.

In other embodiments, eukaryotic host cells, such as yeast, insect, mammalian or plant cells, may be used. Yeast cells, typically *S. cerevisiae*, are useful for eukaryotic genetic studies, due to the ease of targeting genetic changes by homologous recombination and the ability to easily complement genetic defects using recombinantly expressed proteins. Yeast cells are useful for identifying interacting protein components, *e.g.* through use of a two-hybrid system. In a preferred embodiment, yeast cells are useful for protein expression. Vectors of the present invention for use in yeast will typically, but not invariably, contain an origin of replication suitable for use in yeast and a selectable marker that is functional in yeast. Yeast vectors include Yeast Integrating plasmids (*e.g.*, YIp5) and Yeast Replicating plasmids (the YRp and YEpl series plasmids), Yeast Centromere plasmids (the YCp series plasmids), Yeast Artificial Chromosomes (YACs) which are based on yeast linear plasmids, denoted YLp, pGPD-2, 2 μ plasmids and derivatives thereof, and improved shuttle vectors such as those described in Gietz *et al.*, *Gene*, 74:

527-34 (1988) (YIplac, YEplac and YCplac). Selectable markers in yeast vectors include a variety of auxotrophic markers, the most common of which are (in *Saccharomyces cerevisiae*) URA3, HIS3, LEU2, TRP1 and LYS2, which complement specific auxotrophic mutations, such as *ura3-52*, *his3-D1*, *leu2-D1*, *trp1-D1* and *lys2-201*.

5 Insect cells may be chosen for high efficiency protein expression. Where the host cells are from *Spodoptera frugiperda*, e.g., Sf9 and Sf21 cell lines, and expresSF™ cells (Protein Sciences Corp., Meriden, CT, USA), the vector replicative strategy is typically based upon the baculovirus life cycle. Typically, baculovirus transfer vectors are used to replace the wild-type AcMNPV polyhedrin gene with a heterologous gene of interest.

10 Sequences that flank the polyhedrin gene in the wild-type genome are positioned 5' and 3' of the expression cassette on the transfer vectors. Following co-transfection with AcMNPV DNA, a homologous recombination event occurs between these sequences resulting in a recombinant virus carrying the gene of interest and the polyhedrin or p10 promoter. Selection can be based upon visual screening for lacZ fusion activity.

15 The host cells may also be mammalian cells, which are particularly useful for expression of proteins intended as pharmaceutical agents, and for screening of potential agonists and antagonists of a protein or a physiological pathway. Mammalian vectors intended for autonomous extrachromosomal replication will typically include a viral origin, such as the SV40 origin (for replication in cell lines expressing the large T-antigen, such as COS1 and COS7 cells), the papillomavirus origin, or the EBV origin for long term episomal replication (for use, e.g., in 293-EBNA cells, which constitutively express the EBV EBNA-1 gene product and adenovirus E1A). Vectors intended for integration, and thus replication as part of the mammalian chromosome, can, but need not, include an origin of replication functional in mammalian cells, such as the SV40 origin. Vectors
20 based upon viruses, such as adenovirus, adeno-associated virus, vaccinia virus, and various mammalian retroviruses, will typically replicate according to the viral replicative strategy. Selectable markers for use in mammalian cells include, but are not limited to, resistance to neomycin (G418), blasticidin, hygromycin and zeocin, and selection based upon the purine salvage pathway using HAT medium.

30 Expression in mammalian cells can be achieved using a variety of plasmids, including pSV2, pBC12BI, and p91023, as well as lytic virus vectors (e.g., vaccinia virus, adeno virus, and baculovirus), episomal virus vectors (e.g., bovine papillomavirus), and

retroviral vectors (*e.g.*, murine retroviruses). Useful vectors for insect cells include baculoviral vectors and pVL 941.

Plant cells can also be used for expression, with the vector replicon typically derived from a plant virus (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, 5 TMV) and selectable markers chosen for suitability in plants.

It is known that codon usage of different host cells may be different. For example, a plant cell and a human cell may exhibit a difference in codon preference for encoding a particular amino acid. As a result, human mRNA may not be efficiently translated in a plant, bacteria or insect host cell. Therefore, another embodiment of this invention is 10 directed to codon optimization. The codons of the nucleic acid molecules of the invention may be modified to resemble, as much as possible, genes naturally contained within the host cell without altering the amino acid sequence encoded by the nucleic acid molecule.

Any of a wide variety of expression control sequences may be used in these vectors to express the nucleic acid molecules of this invention. Such useful expression 15 control sequences include the expression control sequences associated with structural genes of the foregoing expression vectors. Expression control sequences that control transcription include, *e.g.*, promoters, enhancers and transcription termination sites. Expression control sequences in eukaryotic cells that control post-transcriptional events include splice donor and acceptor sites and sequences that modify the half-life of the 20 transcribed RNA, *e.g.*, sequences that direct poly(A) addition or binding sites for RNA-binding proteins. Expression control sequences that control translation include ribosome binding sites, sequences which direct targeted expression of the polypeptide to or within particular cellular compartments, and sequences in the 5' and 3' untranslated regions that modify the rate or efficiency of translation.

25 Examples of useful expression control sequences for a prokaryote, *e.g.*, *E. coli*, will include a promoter, often a phage promoter, such as phage lambda pL promoter, the trc promoter, a hybrid derived from the trp and lac promoters, the bacteriophage T7 promoter (in *E. coli* cells engineered to express the T7 polymerase), the TAC or TRC system, the major operator and promoter regions of phage lambda, the control regions of 30 fd coat protein, and the araBAD operon. Prokaryotic expression vectors may further include transcription terminators, such as the aspA terminator, and elements that facilitate translation, such as a consensus ribosome binding site and translation termination codon, Schomer *et al.*, *Proc. Natl. Acad. Sci. USA* 83: 8506-8510 (1986).

Expression control sequences for yeast cells, typically *S. cerevisiae*, will include a yeast promoter, such as the CYC1 promoter, the GAL1 promoter, the GAL10 promoter, ADH1 promoter, the promoters of the yeast α -mating system, or the GPD promoter, and will typically have elements that facilitate transcription termination, such as the

5 transcription termination signals from the CYC1 or ADH1 gene.

Expression vectors useful for expressing proteins in mammalian cells will include a promoter active in mammalian cells. These promoters include, but are not limited to, those derived from mammalian viruses, such as the enhancer-promoter sequences from the immediate early gene of the human cytomegalovirus (CMV), the enhancer-promoter

10 sequences from the Rous sarcoma virus long terminal repeat (RSV LTR), the enhancer-promoter from SV40 and the early and late promoters of adenovirus. Other expression control sequences include the promoter for 3-phosphoglycerate kinase or other glycolytic enzymes, the promoters of acid phosphatase. Other expression control sequences include those from the gene comprising the CSNA of interest. Often, expression is enhanced by

15 incorporation of polyadenylation sites, such as the late SV40 polyadenylation site and the polyadenylation signal and transcription termination sequences from the bovine growth hormone (BGH) gene, and ribosome binding sites. Furthermore, vectors can include introns, such as intron II of rabbit β -globin gene and the SV40 splice elements.

Preferred nucleic acid vectors also include a selectable or amplifiable marker gene

20 and means for amplifying the copy number of the gene of interest. Such marker genes are well known in the art. Nucleic acid vectors may also comprise stabilizing sequences (*e.g.*, ori- or ARS-like sequences and telomere-like sequences), or may alternatively be designed to favor directed or non-directed integration into the host cell genome. In a preferred embodiment, nucleic acid sequences of this invention are inserted in frame into an

25 expression vector that allows a high level expression of an RNA which encodes a protein comprising the encoded nucleic acid sequence of interest. Nucleic acid cloning and sequencing methods are well known to those of skill in the art and are described in an assortment of laboratory manuals, including Sambrook (1989), *supra*, Sambrook (2000), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), *supra*. Product information from

30 manufacturers of biological, chemical and immunological reagents also provide useful information.

Expression vectors may be either constitutive or inducible. Inducible vectors include either naturally inducible promoters, such as the *trc* promoter, which is regulated

by the lac operon, and the pL promoter, which is regulated by tryptophan, the MMTV-LTR promoter, which is inducible by dexamethasone, or can contain synthetic promoters and/or additional elements that confer inducible control on adjacent promoters. Examples of inducible synthetic promoters are the hybrid Plac/ara-1 promoter and the

5 PLtetO-1 promoter. The PLtetO-1 promoter takes advantage of the high expression levels from the PL promoter of phage lambda, but replaces the lambda repressor sites with two copies of operator 2 of the Tn10 tetracycline resistance operon, causing this promoter to be tightly repressed by the Tet repressor protein and induced in response to tetracycline (Tc) and Tc derivatives such as anhydrotetracycline. Vectors may also be inducible

10 because they contain hormone response elements, such as the glucocorticoid response element (GRE) and the estrogen response element (ERE), which can confer hormone inducibility where vectors are used for expression in cells having the respective hormone receptors. To reduce background levels of expression, elements responsive to ecdysone, an insect hormone, can be used instead, with coexpression of the ecdysone receptor.

15 In one embodiment of the invention, expression vectors can be designed to fuse the expressed polypeptide to small protein tags that facilitate purification and/or visualization. Such tags include a polyhistidine tag that facilitates purification of the fusion protein by immobilized metal affinity chromatography, for example using NiNTA resin (Qiagen Inc., Valencia, CA, USA) or TALON™ resin (cobalt immobilized affinity chromatography

20 medium, Clontech Labs, Palo Alto, CA, USA). The fusion protein can include a chitin-binding tag and self-excising intein, permitting chitin-based purification with self-removal of the fused tag (IMPACT™ system, New England Biolabs, Inc., Beverly, MA, USA). Alternatively, the fusion protein can include a calmodulin-binding peptide tag, permitting purification by calmodulin affinity resin (Stratagene, La Jolla, CA, USA), or a specifically

25 excisable fragment of the biotin carboxylase carrier protein, permitting purification of *in vivo* biotinylated protein using an avidin resin and subsequent tag removal (Promega, Madison, WI, USA). As another useful alternative, the polypeptides of the present invention can be expressed as a fusion to glutathione-S-transferase, the affinity and specificity of binding to glutathione permitting purification using glutathione affinity

30 resins, such as Glutathione-Superflow Resin (Clontech Laboratories, Palo Alto, CA, USA), with subsequent elution with free glutathione. Other tags include, for example, the Xpress epitope, detectable by anti-Xpress antibody (Invitrogen, Carlsbad, CA, USA), a myc tag, detectable by anti-myc tag antibody, the V5 epitope, detectable by anti-V5

antibody (Invitrogen, Carlsbad, CA, USA), FLAG® epitope, detectable by anti-FLAG® antibody (Stratagene, La Jolla, CA, USA), and the HA epitope, detectable by anti-HA antibody.

For secretion of expressed polypeptides, vectors can include appropriate sequences
5 that encode secretion signals, such as leader peptides. For example, the pSecTag2 vectors (Invitrogen, Carlsbad, CA, USA) are 5.2 kb mammalian expression vectors that carry the secretion signal from the V-J2-C region of the mouse Ig kappa-chain for efficient secretion of recombinant proteins from a variety of mammalian cell lines.

Expression vectors can also be designed to fuse proteins encoded by the
10 heterologous nucleic acid insert to polypeptides that are larger than purification and/or identification tags. Useful protein fusions include those that permit display of the encoded protein on the surface of a phage or cell, fusions to intrinsically fluorescent proteins, such as those that have a green fluorescent protein (GFP)-like chromophore, fusions to the IgG Fc region, and fusions for use in two hybrid systems.

15 Vectors for phage display fuse the encoded polypeptide to, e.g., the gene III protein (pIII) or gene VIII protein (pVIII) for display on the surface of filamentous phage, such as M13. See Barbas *et al.*, Phage Display: A Laboratory Manual, Cold Spring Harbor Laboratory Press (2001); Kay *et al.* (eds.), Phage Display of Peptides and Proteins: A Laboratory Manual, Academic Press, Inc., (1996); Abelson *et al.* (eds.), Combinatorial
20 Chemistry (Methods in Enzymology, Vol. 267) Academic Press (1996). Vectors for yeast display, e.g. the pYD1 yeast display vector (Invitrogen, Carlsbad, CA, USA), use the α -agglutinin yeast adhesion receptor to display recombinant protein on the surface of *S. cerevisiae*. Vectors for mammalian display, e.g., the pDisplay™ vector (Invitrogen, Carlsbad, CA, USA), target recombinant proteins using an N-terminal cell surface
25 targeting signal and a C-terminal transmembrane anchoring domain of platelet derived growth factor receptor.

A wide variety of vectors now exist that fuse proteins encoded by heterologous nucleic acids to the chromophore of the substrate-independent, intrinsically fluorescent green fluorescent protein from *Aequorea victoria* ("GFP") and its variants. The GFP-like
30 chromophore can be selected from GFP-like chromophores found in naturally occurring proteins, such as *A. victoria* GFP (GenBank accession number AAA27721), *Renilla reniformis* GFP, FP583 (GenBank accession no. AF168419) (DsRed), FP593 (AF272711), FP483 (AF168420), FP484 (AF168424), FP595 (AF246709), FP486 (AF168421), FP538

(AF168423), and FP506 (AF168422), and need include only so much of the native protein as is needed to retain the chromophore's intrinsic fluorescence. Methods for determining the minimal domain required for fluorescence are known in the art. *See Li et al., J. Biol. Chem.* 272: 28545-28549 (1997). Alternatively, the GFP-like chromophore can be

5 selected from GFP-like chromophores modified from those found in nature. The methods for engineering such modified GFP-like chromophores and testing them for fluorescence activity, both alone and as part of protein fusions, are well known in the art. *See Heim et al., Curr. Biol.* 6: 178-182 (1996) and *Palm et al., Methods Enzymol.* 302: 378-394 (1999). A variety of such modified chromophores are now commercially available and can readily

10 be used in the fusion proteins of the present invention. These include EGFP ("enhanced GFP"), EBFP ("enhanced blue fluorescent protein"), BFP2, EYFP ("enhanced yellow fluorescent protein"), ECFP ("enhanced cyan fluorescent protein") or Citrine. EGFP (*see, e.g. Cormack et al., Gene* 173: 33-38 (1996); U.S. Patent Nos. 6,090,919 and 5,804,387, the disclosures of which are incorporated herein by reference in their entireties) is found

15 on a variety of vectors, both plasmid and viral, which are available commercially (Clontech Labs, Palo Alto, CA, USA); EBFP is optimized for expression in mammalian cells whereas BFP2, which retains the original jellyfish codons, can be expressed in bacteria (*see, e.g. Heim et al., Curr. Biol.* 6: 178-182 (1996) and *Cormack et al., Gene* 173: 33-38 (1996)). Vectors containing these blue-shifted variants are available from

20 Clontech Labs (Palo Alto, CA, USA). Vectors containing EYFP, ECFP (*see, e.g., Heim et al., Curr. Biol.* 6: 178-182 (1996); *Miyawaki et al., Nature* 388: 882-887 (1997)) and Citrine (*see, e.g., Heikal et al., Proc. Natl. Acad. Sci. USA* 97: 11996-12001 (2000)) are also available from Clontech Labs. The GFP-like chromophore can also be drawn from other modified GFPs, including those described in U.S. Patent Nos. 6,124,128; 6,096,865;

25 6,090,919; 6,066,476; 6,054,321; 6,027,881; 5,968,750; 5,874,304; 5,804,387; 5,777,079; 5,741,668; and 5,625,048, the disclosures of which are incorporated herein by reference in their entireties. *See also Conn (ed.), Green Fluorescent Protein* (Methods in Enzymology, Vol. 302), Academic Press, Inc. (1999); *Yang, et al., J Biol Chem*, 273: 8212-6 (1998); *Bevis et al., Nature Biotechnology*, 20:83-7 (2002). The GFP-like chromophore of each

30 of these GFP variants can usefully be included in the fusion proteins of the present invention.

Fusions to the IgG Fc region increase serum half-life of protein pharmaceutical products through interaction with the FcRn receptor (also denominated the FcRp receptor

and the Brambell receptor, FcRb), further described in International Patent Application Nos. WO 97/43316, WO 97/34631, WO 96/32478, and WO 96/18412, the disclosures of which are incorporated herein by reference in their entireties.

For long-term, high-yield recombinant production of the polypeptides of the present invention, stable expression is preferred. Stable expression is readily achieved by integration into the host cell genome of vectors having selectable markers, followed by selection of these integrants. Vectors such as pUB6/V5-His A, B, and C (Invitrogen, Carlsbad, CA, USA) are designed for high-level stable expression of heterologous proteins in a wide range of mammalian tissue types and cell lines. pUB6/V5-His uses the promoter/enhancer sequence from the human ubiquitin C gene to drive expression of recombinant proteins: expression levels in 293, CHO, and NIH3T3 cells are comparable to levels from the CMV and human EF-1a promoters. The *bsd* gene permits rapid selection of stably transfected mammalian cells with the potent antibiotic blasticidin.

Replication incompetent retroviral vectors, typically derived from Moloney murine leukemia virus, also are useful for creating stable transfectants having integrated provirus. The highly efficient transduction machinery of retroviruses, coupled with the availability of a variety of packaging cell lines such as RetroPack™ PT 67, EcoPack2™-293, AmphoPack-293, and GP2-293 cell lines (all available from Clontech Laboratories, Palo Alto, CA, USA) allow a wide host range to be infected with high efficiency; varying the multiplicity of infection readily adjusts the copy number of the integrated provirus.

Of course, not all vectors and expression control sequences will function equally well to express the nucleic acid molecules of this invention. Neither will all hosts function equally well with the same expression system. However, one of skill in the art may make a selection among these vectors, expression control sequences and hosts without undue experimentation and without departing from the scope of this invention. For example, in selecting a vector, the host must be considered because the vector must be replicated in it. The vector's copy number, the ability to control that copy number, the ability to control integration, if any, and the expression of any other proteins encoded by the vector, such as an antibiotic or other selection marker, should also be considered. The present invention further includes host cells comprising the vectors of the present invention, either present episomally within the cell or integrated, in whole or in part, into the host cell chromosome. Among other considerations, some of which are described above, a host cell strain may be chosen for its ability to process the expressed polypeptide in the desired fashion. Such

post-translational modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation, and it is an aspect of the present invention to provide CSPs with such post-translational modifications.

5 In selecting an expression control sequence, a variety of factors should also be considered. These include, for example, the relative strength of the sequence, its controllability, and its compatibility with the nucleic acid molecules of this invention, particularly with regard to potential secondary structures. Unicellular hosts should be selected by consideration of their compatibility with the chosen vector, the toxicity of the
10 product coded for by the nucleic acid sequences of this invention, their secretion characteristics, their ability to fold the polypeptide correctly, their fermentation or culture requirements, and the ease of purification from them of the products coded for by the nucleic acid molecules of this invention.

The recombinant nucleic acid molecules and more particularly, the expression
15 vectors of this invention may be used to express the polypeptides of this invention as recombinant polypeptides in a heterologous host cell. The polypeptides of this invention may be full-length or less than full-length polypeptide fragments recombinantly expressed from the nucleic acid molecules according to this invention. Such polypeptides include analogs, derivatives and muteins that may or may not have biological activity.

20 Vectors of the present invention will also often include elements that permit *in vitro* transcription of RNA from the inserted heterologous nucleic acid. Such vectors typically include a phage promoter, such as that from T7, T3, or SP6, flanking the nucleic acid insert. Often two different such promoters flank the inserted nucleic acid, permitting separate *in vitro* production of both sense and antisense strands.

25 Transformation and other methods of introducing nucleic acids into a host cell (*e.g.*, conjugation, protoplast transformation or fusion, transfection, electroporation, liposome delivery, membrane fusion techniques, high velocity DNA-coated pellets, viral infection and protoplast fusion) can be accomplished by a variety of methods which are well known in the art (*See*, for instance, Ausubel, *supra*, and Sambrook *et al.*, *supra*).

30 Bacterial, yeast, plant or mammalian cells are transformed or transfected with an expression vector, such as a plasmid, a cosmid, or the like, wherein the expression vector comprises the nucleic acid of interest. Alternatively, the cells may be infected by a viral expression vector comprising the nucleic acid of interest. Depending upon the host cell,

vector, and method of transformation used, transient or stable expression of the polypeptide will be constitutive or inducible. One having ordinary skill in the art will be able to decide whether to express a polypeptide transiently or stably, and whether to express the protein constitutively or inducibly.

- 5 A wide variety of unicellular host cells are useful in expressing the DNA sequences of this invention. These hosts may include well known eukaryotic and prokaryotic hosts, such as strains of, fungi, yeast, insect cells such as *Spodoptera frugiperda* (SF9), animal cells such as CHO, as well as plant cells in tissue culture. Representative examples of appropriate host cells include, but are not limited to, bacterial
- 10 cells, such as *E. coli*, *Caulobacter crescentus*, *Streptomyces* species, and *Salmonella typhimurium*; yeast cells, such as *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Pichia pastoris*, *Pichia methanolica*; insect cell lines, such as those from *Spodoptera frugiperda*, e.g., Sf9 and Sf21 cell lines, and expresSF™ cells (Protein Sciences Corp., Meriden, CT, USA), *Drosophila* S2 cells, and *Trichoplusia ni* High Five® Cells
- 15 (Invitrogen, Carlsbad, CA, USA); and mammalian cells. Typical mammalian cells include BHK cells, BSC 1 cells, BSC 40 cells, BMT 10 cells, VERO cells, COS1 cells, COS7 cells, Chinese hamster ovary (CHO) cells, 3T3 cells, NIH 3T3 cells, 293 cells, HEPG2 cells, HeLa cells, L cells, MDCK cells, HEK293 cells, WI38 cells, murine ES cell lines (e.g., from strains 129/SV, C57/BL6, DBA-1, 129/SVJ), K562 cells, Jurkat cells, and
- 20 BW5147 cells. Other mammalian cell lines are well known and readily available from the American Type Culture Collection (ATCC) (Manassas, VA, USA) and the National Institute of General Medical Sciences (NIGMS) Human Genetic Cell Repository at the Coriell Cell Repositories (Camden, NJ, USA). Cells or cell lines derived from colon are particularly preferred because they may provide a more native post-translational
- 25 processing. Particularly preferred are human colon cells.

Particular details of the transfection, expression and purification of recombinant proteins are well documented and are understood by those of skill in the art. Further details on the various technical aspects of each of the steps used in recombinant production of foreign genes in bacterial cell expression systems can be found in a number

30 of texts and laboratory manuals in the art. See, e.g., Ausubel (1992), *supra*, Ausubel (1999), *supra*, Sambrook (1989), *supra*, and Sambrook (2001), *supra*.

Methods for introducing the vectors and nucleic acid molecules of the present invention into the host cells are well known in the art; the choice of technique will depend primarily upon the specific vector to be introduced and the host cell chosen.

Nucleic acid molecules and vectors may be introduced into prokaryotes, such as *E. coli*, in a number of ways. For instance, phage lambda vectors will typically be packaged using a packaging extract (e.g., Gigapack® packaging extract, Stratagene, La Jolla, CA, USA), and the packaged virus used to infect *E. coli*.

Plasmid vectors will typically be introduced into chemically competent or electrocompetent bacterial cells. *E. coli* cells can be rendered chemically competent by treatment, e.g., with CaCl_2 , or a solution of Mg^{2+} , Mn^{2+} , Ca^{2+} , Rb^+ or K^+ , dimethyl sulfoxide, dithiothreitol, and hexamine cobalt (III), Hanahan, *J. Mol. Biol.* 166(4):557-80 (1983), and vectors introduced by heat shock. A wide variety of chemically competent strains are also available commercially (e.g., Epicurian Coli® XL10-Gold® Ultracompetent Cells (Stratagene, La Jolla, CA, USA); DH5α competent cells (Clontech Laboratories, Palo Alto, CA, USA); and TOP10 Chemically Competent *E. coli* Kit (Invitrogen, Carlsbad, CA, USA)). Bacterial cells can be rendered electrocompetent to take up exogenous DNA by electroporation by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided by BioRad (Richmond, CA, USA).

Vectors can be introduced into yeast cells by spheroplasting, treatment with lithium salts, electroporation, or protoplast fusion. Spheroplasts are prepared by the action of hydrolytic enzymes such as a snail-gut extract, usually denoted Glusulase or Zymolyase, or an enzyme from *Arthrobacter luteus* to remove portions of the cell wall in the presence of osmotic stabilizers, typically 1 M sorbitol. DNA is added to the spheroplasts, and the mixture is co-precipitated with a solution of polyethylene glycol (PEG) and Ca^{2+} . Subsequently, the cells are resuspended in a solution of sorbitol, mixed with molten agar and then layered on the surface of a selective plate containing sorbitol.

For lithium-mediated transformation, yeast cells are treated with lithium acetate to permeabilize the cell wall, DNA is added and the cells are co-precipitated with PEG. The cells are exposed to a brief heat shock, washed free of PEG and lithium acetate, and subsequently spread on plates containing ordinary selective medium. Increased frequencies of transformation are obtained by using specially-prepared single-stranded

carrier DNA and certain organic solvents. Schiestl *et al.*, *Curr. Genet.* 16(5-6): 339-46 (1989).

For electroporation, freshly-grown yeast cultures are typically washed, suspended in an osmotic protectant, such as sorbitol, mixed with DNA, and the cell suspension
5 pulsed in an electroporation device. Subsequently, the cells are spread on the surface of plates containing selective media. Becker *et al.*, *Methods Enzymol.* 194: 182-187 (1991). The efficiency of transformation by electroporation can be increased over 100-fold by using PEG, single-stranded carrier DNA and cells that are in late log-phase of growth. Larger constructs, such as YACs, can be introduced by protoplast fusion.

10 Mammalian and insect cells can be directly infected by packaged viral vectors, or transfected by chemical or electrical means. For chemical transfection, DNA can be coprecipitated with CaPO_4 or introduced using liposomal and nonliposomal lipid-based agents. Commercial kits are available for CaPO_4 transfection (CalPhos™ Mammalian Transfection Kit, Clontech Laboratories, Palo Alto, CA, USA), and lipid-mediated
15 transfection can be practiced using commercial reagents, such as LIPOFECTAMINE™ 2000, LIPOFECTAMINE™ Reagent, CELLFECTIN® Reagent, and LIPOFECTIN® Reagent (Invitrogen, Carlsbad, CA, USA), DOTAP Liposomal Transfection Reagent, FuGENE 6, X-tremeGENE Q2, DOSPER, (Roche Molecular Biochemicals, Indianapolis, IN USA), Effectene™, PolyFect®, Superfect® (Qiagen, Inc., Valencia, CA, USA).
20 Protocols for electroporating mammalian cells can be found in, for example, ; Norton *et al.* (eds.), Gene Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechniques Books, Eaton Publishing Co. (2000). Other transfection techniques include transfection by particle bombardment and microinjection. See, e.g., Cheng *et al.*, *Proc. Natl. Acad. Sci. USA* 90(10): 4455-9 (1993); Yang *et al.*, *Proc. Natl. Acad. Sci. USA*
25 87(24): 9568-72 (1990).

Production of the recombinantly produced proteins of the present invention can optionally be followed by purification.

Purification of recombinantly expressed proteins is now well within the skill in the art and thus need not be detailed here. See, e.g., Thorner *et al.* (eds.), Applications of
30 Chimeric Genes and Hybrid Proteins, Part A: Gene Expression and Protein Purification (Methods in Enzymology, Vol. 326), Academic Press (2000); Harbin (ed.), Cloning, Gene Expression and Protein Purification : Experimental Procedures and Process Rationale, Oxford Univ. Press (2001); Marshak *et al.*, Strategies for Protein Purification and

Characterization: A Laboratory Course Manual, Cold Spring Harbor Laboratory Press (1996); and Roe (ed.), Protein Purification Applications, Oxford University Press (2001).

Briefly, however, if purification tags have been fused through use of an expression vector that appends such tags, purification can be effected, at least in part, by means
5 appropriate to the tag, such as use of immobilized metal affinity chromatography for polyhistidine tags. Other techniques common in the art include ammonium sulfate fractionation, immunoprecipitation, fast protein liquid chromatography (FPLC), high performance liquid chromatography (HPLC), and preparative gel electrophoresis.

10 Polypeptides, including Fragments Muteins, Homologous Proteins, Allelic Variants, Analogs and Derivatives

Another aspect of the invention relates to polypeptides encoded by the nucleic acid molecules described herein. In a preferred embodiment, the polypeptide is a colon specific polypeptide (CSP). In an even more preferred embodiment, the polypeptide comprises an amino acid sequence of SEQ ID NO:95-248 or is derived from a polypeptide
15 having the amino acid sequence of SEQ ID NO: 95-248. A polypeptide as defined herein may be produced recombinantly, as discussed *supra*, may be isolated from a cell that naturally expresses the protein, or may be chemically synthesized following the teachings of the specification and using methods well known to those having ordinary skill in the art.

Polypeptides of the present invention may also comprise a part or fragment of a
20 CSP. In a preferred embodiment, the fragment is derived from a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 95-248. Polypeptides of the present invention comprising a part or fragment of an entire CSP may or may not be CSPs. For example, a full-length polypeptide may be colon-specific, while a fragment thereof may be found in other tissues as well as in colon. A polypeptide that is
25 not a CSP, whether it is a fragment, analog, mutein, homologous protein or derivative, is nevertheless useful, especially for immunizing animals to prepare anti-CSP antibodies. In a preferred embodiment, the part or fragment is a CSP. Methods of determining whether a polypeptide of the present invention is a CSP are described *infra*.

Polypeptides of the present invention comprising fragments of at least 6
30 contiguous amino acids are also useful in mapping B cell and T cell epitopes of the reference protein. See, e.g., Geysen *et al.*, *Proc. Natl. Acad. Sci. USA* 81: 3998-4002 (1984) and U.S. Patent Nos. 4,708,871 and 5,595,915, the disclosures of which are

incorporated herein by reference in their entireties. Because the fragment need not itself be immunogenic, part of an immunodominant epitope, nor even recognized by native antibody, to be useful in such epitope mapping, all fragments of at least 6 amino acids of a polypeptide of the present invention have utility in such a study.

5 Polypeptides of the present invention comprising fragments of at least 8 contiguous amino acids, often at least 15 contiguous amino acids, are useful as immunogens for raising antibodies that recognize polypeptides of the present invention. *See, e.g.,* Lerner, *Nature* 299: 592-596 (1982); Shinnick *et al.*, *Annu. Rev. Microbiol.* 37: 425-46 (1983); Sutcliffe *et al.*, *Science* 219: 660-6 (1983). As further described in the
10 above-cited references, virtually all 8-mers, conjugated to a carrier, such as a protein, prove immunogenic and are capable of eliciting antibody for the conjugated peptide; accordingly, all fragments of at least 8 amino acids of the polypeptides of the present invention have utility as immunogens.

Polypeptides comprising fragments of at least 8, 9, 10 or 12 contiguous amino
15 acids are also useful as competitive inhibitors of binding of the entire polypeptide, or a portion thereof, to antibodies (as in epitope mapping), and to natural binding partners, such as subunits in a multimeric complex or to receptors or ligands of the subject protein; this competitive inhibition permits identification and separation of molecules that bind specifically to the polypeptide of interest. *See* U.S. Patent Nos. 5,539,084 and 5,783,674,
20 incorporated herein by reference in their entireties.

The polypeptide of the present invention thus preferably is at least 6 amino acids in length, typically at least 8, 9, 10 or 12 amino acids in length, and often at least 15 amino acids in length. Often, the polypeptide of the present invention is at least 20 amino acids in length, even 25 amino acids, 30 amino acids, 35 amino acids, or 50 amino acids or more
25 in length. Of course, larger polypeptides having at least 75 amino acids, 100 amino acids, or even 150 amino acids are also useful, and at times preferred.

One having ordinary skill in the art can produce fragments by truncating the nucleic acid molecule, *e.g.*, a CSNA, encoding the polypeptide and then expressing it recombinantly. Alternatively, one can produce a fragment by chemically synthesizing a
30 portion of the full-length polypeptide. One may also produce a fragment by enzymatically cleaving either a recombinant polypeptide or an isolated naturally occurring polypeptide. Methods of producing polypeptide fragments are well known in the art. *See, e.g.,* Sambrook (1989), *supra*; Sambrook (2001), *supra*; Ausubel (1992), *supra*; and Ausubel

(1999), *supra*. In one embodiment, a polypeptide comprising only a fragment, preferably a fragment of a CSP, may be produced by chemical or enzymatic cleavage of a CSP polypeptide. In a preferred embodiment, a polypeptide fragment is produced by expressing a nucleic acid molecule of the present invention encoding a fragment,
5 preferably of a CSP, in a host cell.

Polypeptides of the present invention are also inclusive of mutants, fusion proteins, homologous proteins and allelic variants.

A mutant protein, or mutein, may have the same or different properties compared to a naturally occurring polypeptide and comprises at least one amino acid insertion,
10 duplication, deletion, rearrangement or substitution compared to the amino acid sequence of a native polypeptide. Small deletions and insertions can often be found that do not alter the function of a protein. Muteins may or may not be colon-specific. Preferably, the mutein is colon-specific. More preferably the mutein is a polypeptide that comprises at least one amino acid insertion, duplication, deletion, rearrangement or substitution
15 compared to the amino acid sequence of SEQ ID NO: 95-248. Accordingly, in a preferred embodiment, the mutein is one that exhibits at least 50% sequence identity, more preferably at least 60% sequence identity, even more preferably at least 70%, yet more preferably at least 80% sequence identity to a CSP comprising an amino acid sequence of SEQ ID NO: 95-248. In a yet more preferred embodiment, the mutein exhibits at least
20 85%, more preferably 90%, even more preferably 95% or 96%, and yet more preferably at least 97%, 98%, 99% or 99.5% sequence identity to a CSP comprising an amino acid sequence of SEQ ID NO: 95-248.

A mutein may be produced by isolation from a naturally occurring mutant cell, tissue or organism. A mutein may be produced by isolation from a cell, tissue or organism
25 that has been experimentally mutagenized. Alternatively, a mutein may be produced by chemical manipulation of a polypeptide, such as by altering the amino acid residue to another amino acid residue using synthetic or semi-synthetic chemical techniques. In a preferred embodiment, a mutein is produced from a host cell comprising a mutated nucleic acid molecule compared to the naturally occurring nucleic acid molecule. For instance,
30 one may produce a mutein of a polypeptide by introducing one or more mutations into a nucleic acid molecule of the invention and then expressing it recombinantly. These mutations may be targeted, in which particular encoded amino acids are altered, or may be untargeted, in which random encoded amino acids within the polypeptide are altered.

Mutagens with random amino acid alterations can be screened for a particular biological activity or property, particularly whether the polypeptide is colon-specific, as described below. Multiple random mutations can be introduced into the gene by methods well known to the art, *e.g.*, by error-prone PCR, shuffling, oligonucleotide-directed
5 mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis and site-specific mutagenesis. Methods of producing mutagens with targeted or random amino acid alterations are well known in the art. *See, e.g.*, Sambrook (1989), *supra*; Sambrook (2001), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), as well as U.S. Patent No.
10 5,223,408, which is herein incorporated by reference in its entirety.

The invention also contemplates polypeptides that are homologous to a polypeptide of the invention. In a preferred embodiment, the polypeptide is homologous to a CSP. In an even more preferred embodiment, the polypeptide is homologous to a CSP selected from the group having an amino acid sequence of SEQ ID NO: 95-248. By
15 homologous polypeptide it is meant one that exhibits significant sequence identity to a CSP, preferably a CSP having an amino acid sequence of SEQ ID NO: 95-248. By significant sequence identity it is meant that the homologous polypeptide exhibits at least 50% sequence identity, more preferably at least 60% sequence identity, even more preferably at least 70%, yet more preferably at least 80% sequence identity to a CSP
20 comprising an amino acid sequence of SEQ ID NO: 95-248. More preferred are homologous polypeptides exhibiting at least 85%, more preferably 90%, even more preferably 95% or 96%, and yet more preferably at least 97% or 98% sequence identity to a CSP comprising an amino acid sequence of SEQ ID NO: 95-248. Most preferably, the homologous polypeptide exhibits at least 99%, more preferably 99.5%, even more
25 preferably 99.6%, 99.7%, 99.8% or 99.9% sequence identity to a CSP comprising an amino acid sequence of SEQ ID NO: 95-248. In a preferred embodiment, the amino acid substitutions of the homologous polypeptide are conservative amino acid substitutions as discussed *supra*.

Homologous polypeptides of the present invention also comprise polypeptide
30 encoded by a nucleic acid molecule that selectively hybridizes to a CSNA or an antisense sequence thereof. In this embodiment, it is preferred that the homologous polypeptide be encoded by a nucleic acid molecule that hybridizes to a CSNA under low stringency, moderate stringency or high stringency conditions, as defined herein. More preferred is a

homologous polypeptide encoded by a nucleic acid sequence which hybridizes to a CSNA selected from the group consisting of SEQ ID NO: 1-94 or a homologous polypeptide encoded by a nucleic acid molecule that hybridizes to a nucleic acid molecule that encodes a CSP, preferably a CSP of SEQ ID NO:95-248 under low stringency, moderate
5 stringency or high stringency conditions, as defined herein.

Homologous polypeptides of the present invention may be naturally occurring and derived from another species, especially one derived from another primate, such as chimpanzee, gorilla, rhesus macaque, or baboon, wherein the homologous polypeptide comprises an amino acid sequence that exhibits significant sequence identity to that of
10 SEQ ID NO: 95-248. The homologous polypeptide may also be a naturally occurring polypeptide from a human, when the CSP is a member of a family of polypeptides. The homologous polypeptide may also be a naturally occurring polypeptide derived from a non-primate, mammalian species, including without limitation, domesticated species, *e.g.*, dog, cat, mouse, rat, rabbit, guinea pig, hamster, cow, horse, goat or pig. The homologous
15 polypeptide may also be a naturally occurring polypeptide derived from a non-mammalian species, such as birds or reptiles. The naturally occurring homologous protein may be isolated directly from humans or other species. Alternatively, the nucleic acid molecule encoding the naturally occurring homologous polypeptide may be isolated and used to express the homologous polypeptide recombinantly. The homologous polypeptide may
20 also be one that is experimentally produced by random mutation of a nucleic acid molecule and subsequent expression of the nucleic acid molecule. Alternatively, the homologous polypeptide may be one that is experimentally produced by directed mutation of one or more codons to alter the encoded amino acid of a CSP. In a preferred embodiment, the homologous polypeptide encodes a polypeptide that is a CSP.

25 Relatedness of proteins can also be characterized using a second functional test, such as the ability of a first protein competitively to inhibit the binding of a second protein to an antibody. It is, therefore, another aspect of the present invention to provide isolated polypeptides not only identical in sequence to those described with particularity herein, but also to provide isolated polypeptides ("cross-reactive proteins") that competitively inhibit
30 the binding of antibodies to all or to a portion of the isolated polypeptides of the present invention. Such competitive inhibition can readily be determined using immunoassays well known in the art.

As discussed above, single nucleotide polymorphisms (SNPs) occur frequently in eukaryotic genomes, and the sequence determined from one individual of a species may differ from other allelic forms present within the population. Thus, polypeptides of the present invention are also inclusive of those encoded by an allelic variant of a nucleic acid molecule encoding a CSP. In this embodiment, it is preferred that the polypeptide be encoded by an allelic variant of a gene that encodes a polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO: 95-248. More preferred is that the polypeptide be encoded by an allelic variant of a gene that has the nucleic acid sequence selected from the group consisting of SEQ ID NO: 1-94.

Polypeptides of the present invention are also inclusive of derivative polypeptides encoded by a nucleic acid molecule according to the instant invention. In this embodiment, it is preferred that the polypeptide be a CSP. Also preferred are derivative polypeptides having an amino acid sequence selected from the group consisting of SEQ ID NO: 95-248 and which has been acetylated, carboxylated, phosphorylated, glycosylated, ubiquitinated or post-translationally modified in another manner. In another preferred embodiment, the derivative has been labeled with, *e.g.*, radioactive isotopes such as ^{125}I , ^{32}P , ^{35}S , and ^3H . In another preferred embodiment, the derivative has been labeled with fluorophores, chemiluminescent agents, enzymes, and antiligands that can serve as specific binding pair members for a labeled ligand.

Polypeptide modifications are well known to those of skill and have been described in great detail in the scientific literature. Several particularly common modifications, glycosylation, lipid attachment, sulfation, gamma-carboxylation of glutamic acid residues, hydroxylation and ADP-ribosylation, for instance, are described in most basic texts, such as, for instance Creighton, Protein Structure and Molecular Properties, 2nd ed., W. H. Freeman and Company (1993). Many detailed reviews are available on this subject, such as, for example, those provided by Wold, in Johnson (ed.), Posttranslational Covalent Modification of Proteins, pgs. 1-12, Academic Press (1983); Seifter *et al.*, *Meth. Enzymol.* 182: 626-646 (1990) and Rattan *et al.*, *Ann. N.Y. Acad. Sci.* 663: 48-62 (1992).

One may determine whether a polypeptide of the invention is likely to be post-translationally modified by analyzing the sequence of the polypeptide to determine if there are peptide motifs indicative of sites for post-translational modification. There are a number of computer programs that permit prediction of post-translational modifications.

See, e.g., expasy.org (accessed November 11, 2002) on the world wide web, which includes PSORT, for prediction of protein sorting signals and localization sites, SignalP, for prediction of signal peptide cleavage sites, MITOPROT and Predotar, for prediction of mitochondrial targeting sequences, NetOGlyc, for prediction of type O-glycosylation sites
 5 in mammalian proteins, big-PI Predictor and DGPI, for prediction of prenylation-anchor and cleavage sites, and NetPhos, for prediction of Ser, Thr and Tyr phosphorylation sites in eukaryotic proteins. Other computer programs, such as those included in GCG, also may be used to determine post-translational modification peptide motifs.

General examples of types of post-translational modifications include, but are not
 10 limited to: (Z)-dehydrobutyryne; 1-chondroitin sulfate-L-aspartic acid ester; 1'-glycosyl-L-tryptophan; 1'-phospho-L-histidine; 1-thioglycine; 2'-(S-L-cysteinyl)-L-histidine; 2'-[3-carboxamido (trimethylammonio)propyl]-L-histidine; 2'-alpha-mannosyl-L-tryptophan; 2-methyl-L-glutamine; 2-oxobutanoic acid; 2-pyrrolidone carboxylic acid; 3'-(1'-L-histidyl)-L-tyrosine; 3'-(8alpha-FAD)-L-histidine; 3'-(S-L-cysteinyl)-L-tyrosine; 3', 3'', 5'-triiodo-L-
 15 thyronine; 3'-4'-phospho-L-tyrosine; 3-hydroxy-L-proline; 3'-methyl-L-histidine; 3-methyl-L-lanthionine; 3'-phospho-L-histidine; 4'-(L-tryptophan)-L-tryptophyl quinone; 42 N-cysteinyl-glycosylphosphatidylinositol ethanolamine; 43 -(T-L-histidyl)-L-tyrosine; 4-hydroxy-L-arginine; 4-hydroxy-L-lysine; 4-hydroxy-L-proline; 5'-(N6-L-lysine)-L-topaquinone; 5-hydroxy-L-lysine; 5-methyl-L-arginine; alpha-I-microglobulin-Ig alpha
 20 complex chromophore; bis-L-cysteinyl bis-L-histidino diiron disulfide; bis-L--cysteinyl-L-N3'-histidino-L-serinyl tetrairon' tetrasulfide; chondroitin sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-serine; D-alanine; D-allo-isoleucine; D-asparagine; dehydroalanine; dehydrotyrosine; dermatan 4-sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-serine; D-glucuronyl-N-glycine; dipyrrolylmethanemethyl-L-
 25 cysteine; D-leucine; D-methionine; D-phenylalanine; D-serine; D-tryptophan; glycine amide; glycine oxazolecarboxylic acid; glycine thiazolecarboxylic acid; heme P450-bis-L-cysteine-L-tyrosine; heme-bis-L-cysteine; hemediol-L-aspartyl ester-L-glutamyl ester; hemediol-L-aspartyl ester-L-glutamyl ester-L-methionine sulfonium; heme-L-cysteine; heme-L-histidine; heparan sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-
 30 serine; heme P450-bis-L-cysteine-L-lysine; hexakis-L-cysteinyl hexairon hexasulfide; keratan sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-threonine; L-oxoalanine- lactic acid; L phenyllactic acid; 1'-(8alpha-FAD)-L-histidine; L-2'.4'.5'-topaquinone; L-3'.4'.5'-trihydroxyphenylalanine; L-3'.4'.5'-trihydroxyphenylalanine; L-4'-

- bromophenylalanine; L-6'-bromotryptophan; L-alanine amide; L-alanyl imidazolinone glycine; L-allysine; L-arginine amide; L-asparagine amide; L-aspartic 4-phosphoric anhydride; L-aspartic acid 1-amide; L-beta-methylthioaspartic acid; L-bromohistidine; L-citrulline; L-cysteine amide; L-cysteine glutathione disulfide; L-cysteine methyl disulfide;
- 5 L-cysteine methyl ester; L-cysteine oxazolecarboxylic acid; L-cysteine oxazolinecarboxylic acid; L-cysteine persulfide; L-cysteine sulfenic acid; L-cysteine sulfinic acid; L-cysteine thiazolecarboxylic acid; L-cysteinyl homocitryl molybdenum-heptairon-nonasulfide; L-cysteinyl imidazolinone glycine; L-cysteinyl molybdopterin; L-cysteinyl molybdopterin guanine dinucleotide; L-cystine; L-erythro-beta-
- 10 hydroxyasparagine; L-erythro-beta-hydroxyaspartic acid; L-gamma-carboxyglutamic acid; L-glutamic acid 1-amide; L-glutamic acid 5-methyl ester; L-glutamine amide; L-glutamyl 5-glycerylphosphorylethanolamine; L-histidine amide; L-isoglutamyl-polyglutamic acid; L-isoglutamyl-polyglycine; L-isoleucine amide; L-lanthionine; L-leucine amide; L-lysine amide; L-lysine thiazolecarboxylic acid; L-lysinoalanine; L-methionine amide; L-
- 15 methionine sulfone; L-phenylalanine thiazolecarboxylic acid; L-phenylalanine amide; L-proline amide; L-selenocysteine; L-selenocysteinyl molybdopterin guanine dinucleotide; L-serine amide; L-serine thiazolecarboxylic acid; L-seryl imidazolinone glycine; L-T-bromophenylalanine; L-T-bromophenylalanine; L-threonine amide; L-thyroxine; L-tryptophan amide; L-tryptophyl quinone; L-tyrosine amide; L-valine amide; meso-
- 20 lanthionine; N-(L-glutamyl)-L-tyrosine; N-(L-isoaspartyl)-glycine; N-(L-isoaspartyl)-L-cysteine; N,N,N-trimethyl-L-alanine; N,N-dimethyl-L-proline; N2-acetyl-L-lysine; N2-succinyl-L-tryptophan; N4-(ADP-ribosyl)-L-asparagine; N4-glycosyl-L-asparagine; N4-hydroxymethyl-L-asparagine; N4-methyl-L-asparagine; N5-methyl-L-glutamine; N6-1-carboxyethyl-L-lysine; N6-(4-amino hydroxybutyl)-L-lysine; N6-(L-isoglutamyl)-L-
- 25 lysine; N6-(phospho-5'-adenosine)-L-lysine; N6-(phospho-5'-guanosine)-L-lysine; N6,N6,N6-trimethyl-L-lysine; N6,N6-dimethyl-L-lysine; N6-acetyl-L-lysine; N6-biotinyl-L-lysine; N6-carboxy-L-lysine; N6-formyl-L-lysine; N6-glycyl-L-lysine; N6-lipoyl-L-lysine; N6-methyl-L-lysine; N6-methyl-N6-poly(N-methyl-propylamine)-L-lysine; N6-mureinyl-L-lysine; N6-myristoyl-L-lysine; N6-palmitoyl-L-lysine; N6-pyridoxal
- 30 phosphate-L-lysine; N6-pyruvic acid 2-iminyl-L-lysine; N6-retinal-L-lysine; N-acetylglycine; N-acetyl-L-glutamine; N-acetyl-L-alanine; N-acetyl-L-aspartic acid; N-acetyl-L-cysteine; N-acetyl-L-glutamic acid; N-acetyl-L-isoleucine; N-acetyl-L-methionine; N-acetyl-L-proline; N-acetyl-L-serine; N-acetyl-L-threonine; N-acetyl-L-

tyrosine; N-acetyl-L-valine; N-alanyl-glycosylphosphatidylinositoethanolamine; N-asparaginy-
 l-glycosylphosphatidylinositoethanolamine; N-aspartyl-
 glycosylphosphatidylinositoethanolamine; N-formylglycine; N-formyl-L-methionine; N-
 glycyl-glycosylphosphatidylinositoethanolamine; N-L-glutamyl-poly-L-glutamic acid; N-
 5 methylglycine; N-methyl-L-alanine; N-methyl-L-methionine; N-methyl-L-phenylalanine;
 N-myristoyl-glycine; N-palmitoyl-L-cysteine; N-pyruvic acid 2-iminyl-L-cysteine; N-
 pyruvic acid 2-iminyl-L-valine; N-seryl-glycosylphosphatidylinositoethanolamine; N-
 seryl-glycosylphosphatidylinositoethanolamine; O-(ADP-ribosyl)-L-serine; O-(phospho-
 5'-adenosine)-L-threonine; O-(phospho-5'-DNA)-L-serine; O-(phospho-5'-DNA)-L-
 10 threonine; O-(phospho-5'rRNA)-L-serine; O-(phosphoribosyl dephospho-coenzyme A)-L-
 serine; O-(sn-1-glycerophosphoryl)-L-serine; O4'-(8alpha-FAD)-L-tyrosine; O4'-(phospho-
 5'-adenosine)-L-tyrosine; O4'-(phospho-5'-DNA)-L-tyrosine; O4'-(phospho-5'-RNA)-L-
 tyrosine; O4'-(phospho-5'-uridine)-L-tyrosine; O4-glycosyl-L-hydroxyproline; O4'-
 glycosyl-L-tyrosine; O4'-sulfo-L-tyrosine; O5-glycosyl-L-hydroxylysine; O-glycosyl-L-
 15 serine; O-glycosyl-L-threonine; omega-N-(ADP-ribosyl)-L-arginine; omega-N-omega-N'-
 dimethyl-L-arginine; omega-N-methyl-L-arginine; omega-N-omega-N-dimethyl-L-
 arginine; omega-N-phospho-L-arginine; O-octanoyl-L-serine; O-palmitoyl-L-serine; O-
 palmitoyl-L-threonine; O-phospho-L-serine; O-phospho-L-threonine; O-
 phosphopantetheine-L-serine; phycoerythrobilin-bis-L-cysteine; phycourobilin-bis-L-
 20 cysteine; pyrroloquinoline quinone; pyruvic acid; S hydroxycinnamyl-L-cysteine; S-(2-
 aminovinyl) methyl-D-cysteine; S-(2-aminovinyl)-D-cysteine; S-(6-FW-L-cysteine; S-
 (8alpha-FAD)-L-cysteine; S-(ADP-ribosyl)-L-cysteine; S-(L-isoglutamyl)-L-cysteine; S-
 12-hydroxyfarnesyl-L-cysteine; S-acetyl-L-cysteine; S-diacylglycerol-L-cysteine; S-
 diphytanylglycerol diether-L-cysteine; S-farnesyl-L-cysteine; S-geranylgeranyl-L-
 25 cysteine; S-glycosyl-L-cysteine; S-glycyl-L-cysteine; S-methyl-L-cysteine; S-nitrosyl-L-
 cysteine; S-palmitoyl-L-cysteine; S-phospho-L-cysteine; S-phycobiliviolin-L-cysteine; S-
 phycocyanobilin-L-cysteine; S-phycoerythrobilin-L-cysteine; S-phytochromobilin-L-
 cysteine; S-selenyl-L-cysteine; S-sulfo-L-cysteine; tetrakis-L-cysteinyl diiron disulfide;
 tetrakis-L-cysteinyl iron; tetrakis-L-cysteinyl tetrairon tetrasulfide; trans-2,3-cis 4-
 30 dihydroxy-L-proline; tris-L-cysteinyl triiron tetrasulfide; tris-L-cysteinyl triiron trisulfide;
 tris-L-cysteinyl-L-aspartato tetrairon tetrasulfide; tris-L-cysteinyl-L-cysteine persulfido-
 bis-L-glutamato-L-histidino tetrairon disulfide trioxide; tris-L-cysteinyl-L-N3'-histidino

tetrairon tetrasulfide; tris-L-cysteinyl-L-Nl'-histidino tetrairon tetrasulfide; and tris-L-cysteinyl-L-serinyl tetrairon tetrasulfide.

Additional examples of PTMs may be found in web sites such as the Delta Mass database based on Krishna, R. G. and F. Wold (1998). Posttranslational Modifications.

- 5 Proteins - Analysis and Design. R. H. Angeletti. San Diego, Academic Press. 1: 121-206; Methods in Enzymology, 193, J.A. McClosky (ed) (1990), pages 647-660; Methods in Protein Sequence Analysis edited by Kazutomo Imahori and Fumio Sakiyama, Plenum Press, (1993) "Post-translational modifications of proteins" R.G. Krishna and F. Wold pages 167-172; "GlycoSuiteDB: a new curated relational database of glycoprotein glycan
10 structures and their biological sources" Cooper et al. Nucleic Acids Res. 29; 332-335 (2001) "O-GLYCBASE version 4.0: a revised database of O-glycosylated proteins" Gupta et al. Nucleic Acids Research, 27: 370-372 (1999); and "PhosphoBase, a database of phosphorylation sites: release 2.0.", Kreegipuu et al. Nucleic Acids Res 27(1):237-239 (1999) see also, WO 02/21139A2, the disclosure of which is incorporated herein by
15 reference in its entirety.

- Tumorigenesis is often accompanied by alterations in the post-translational modifications of proteins. Thus, in another embodiment, the invention provides polypeptides from cancerous cells or tissues that have altered post-translational modifications compared to the post-translational modifications of polypeptides from
20 normal cells or tissues. A number of altered post-translational modifications are known. One common alteration is a change in phosphorylation state, wherein the polypeptide from the cancerous cell or tissue is hyperphosphorylated or hypophosphorylated compared to the polypeptide from a normal tissue, or wherein the polypeptide is phosphorylated on different residues than the polypeptide from a normal cell. Another common alteration is
25 a change in glycosylation state, wherein the polypeptide from the cancerous cell or tissue has more or less glycosylation than the polypeptide from a normal tissue, and/or wherein the polypeptide from the cancerous cell or tissue has a different type of glycosylation than the polypeptide from a noncancerous cell or tissue. Changes in glycosylation may be critical because carbohydrate-protein and carbohydrate-carbohydrate interactions are
30 important in cancer cell progression, dissemination and invasion. See, e.g., Barchi, *Curr. Pharm. Des.* 6: 485-501 (2000), Verma, *Cancer Biochem. Biophys.* 14: 151-162 (1994) and Dennis et al., *Bioessays* 5: 412-421 (1999).

Another post-translational modification that may be altered in cancer cells is prenylation. Prenylation is the covalent attachment of a hydrophobic prenyl group (either farnesyl or geranylgeranyl) to a polypeptide. Prenylation is required for localizing a protein to a cell membrane and is often required for polypeptide function. For instance, the Ras superfamily of GTPase signalling proteins must be prenylated for function in a cell. See, e.g., Prendergast et al., *Semin. Cancer Biol.* 10: 443-452 (2000) and Khwaja et al., *Lancet* 355: 741-744 (2000).

Other post-translation modifications that may be altered in cancer cells include, without limitation, polypeptide methylation, acetylation, arginylation or racemization of amino acid residues. In these cases, the polypeptide from the cancerous cell may exhibit either increased or decreased amounts of the post-translational modification compared to the corresponding polypeptides from noncancerous cells.

Other polypeptide alterations in cancer cells include abnormal polypeptide cleavage of proteins and aberrant protein-protein interactions. Abnormal polypeptide cleavage may be cleavage of a polypeptide in a cancerous cell that does not usually occur in a normal cell, or a lack of cleavage in a cancerous cell, wherein the polypeptide is cleaved in a normal cell. Aberrant protein-protein interactions may be either covalent cross-linking or non-covalent binding between proteins that do not normally bind to each other. Alternatively, in a cancerous cell, a protein may fail to bind to another protein to which it is bound in a noncancerous cell. Alterations in cleavage or in protein-protein interactions may be due to over- or underproduction of a polypeptide in a cancerous cell compared to that in a normal cell, or may be due to alterations in post-translational modifications (see above) of one or more proteins in the cancerous cell. See, e.g., Henschen-Edman, *Ann. N.Y. Acad. Sci.* 936: 580-593 (2001).

Alterations in polypeptide post-translational modifications, as well as changes in polypeptide cleavage and protein-protein interactions, may be determined by any method known in the art. For instance, alterations in phosphorylation may be determined by using anti-phosphoserine, anti-phosphothreonine or anti-phosphotyrosine antibodies or by amino acid analysis. Glycosylation alterations may be determined using antibodies specific for different sugar residues, by carbohydrate sequencing, or by alterations in the size of the glycoprotein, which can be determined by, e.g., SDS polyacrylamide gel electrophoresis (PAGE). Other alterations of post-translational modifications, such as prenylation, racemization, methylation, acetylation and arginylation, may be determined by chemical

analysis, protein sequencing, amino acid analysis, or by using antibodies specific for the particular post-translational modifications. Changes in protein-protein interactions and in polypeptide cleavage may be analyzed by any method known in the art including, without limitation, non-denaturing PAGE (for non-covalent protein-protein interactions), SDS
5 PAGE (for covalent protein-protein interactions and protein cleavage), chemical cleavage, protein sequencing or immunoassays.

In another embodiment, the invention provides polypeptides that have been post-translationally modified. In one embodiment, polypeptides may be modified enzymatically or chemically, by addition or removal of a post-translational modification.
10 For example, a polypeptide may be glycosylated or deglycosylated enzymatically. Similarly, polypeptides may be phosphorylated using a purified kinase, such as a MAP kinase (e.g., p38, ERK, or JNK) or a tyrosine kinase (e.g., Src or erbB2). A polypeptide may also be modified through synthetic chemistry. Alternatively, one may isolate the polypeptide of interest from a cell or tissue that expresses the polypeptide with the desired
15 post-translational modification. In another embodiment, a nucleic acid molecule encoding the polypeptide of interest is introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide in the desired fashion. If the polypeptide does not contain a motif for a desired post-translational modification, one may alter the post-translational modification by mutating the nucleic acid sequence of a nucleic
20 acid molecule encoding the polypeptide so that it contains a site for the desired post-translational modification. Amino acid sequences that may be post-translationally modified are known in the art. See, e.g., the programs described above on the website expasy.org of the world wide web. The nucleic acid molecule may also be introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide.
25 Similarly, one may delete sites that are post-translationally modified by either mutating the nucleic acid sequence so that the encoded polypeptide does not contain the post-translational modification motif, or by introducing the native nucleic acid molecule into a host cell that is not capable of post-translationally modifying the encoded polypeptide.

It will be appreciated, as is well known and as noted above, that polypeptides are
30 not always entirely linear. For instance, polypeptides may be branched as a result of ubiquitination, and they may be circular, with or without branching, generally as a result of posttranslation events, including natural processing events and events brought about by human manipulation which do not occur naturally. Circular, branched and branched

circular polypeptides may be synthesized by non-translation natural processes and by entirely synthetic methods, as well. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. In fact, blockage of the amino or carboxyl group in a polypeptide, or both, by a covalent modification, is common in naturally occurring and synthetic polypeptides and such modifications may be present in polypeptides of the present invention, as well. For instance, the amino terminal residue of polypeptides made in *E. coli*, prior to proteolytic processing, almost invariably will be N-formylmethionine.

Useful post-synthetic (and post-translational) modifications include conjugation to detectable labels, such as fluorophores. A wide variety of amine-reactive and thiol-reactive fluorophore derivatives have been synthesized that react under nondenaturing conditions with N-terminal amino groups and epsilon amino groups of lysine residues, on the one hand, and with free thiol groups of cysteine residues, on the other.

Kits are available commercially that permit conjugation of proteins to a variety of amine-reactive or thiol-reactive fluorophores: Molecular Probes, Inc. (Eugene, OR, USA), *e.g.*, offers kits for conjugating proteins to Alexa Fluor 350, Alexa Fluor 430, Fluorescein-EX, Alexa Fluor 488, Oregon Green 488, Alexa Fluor 532, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, and Texas Red-X.

A wide variety of other amine-reactive and thiol-reactive fluorophores are available commercially (Molecular Probes, Inc., Eugene, OR, USA), including Alexa Fluor® 350, Alexa Fluor® 488, Alexa Fluor® 532, Alexa Fluor® 546, Alexa Fluor® 568, Alexa Fluor® 594, Alexa Fluor® 647 (monoclonal antibody labeling kits available from Molecular Probes, Inc., Eugene, OR, USA), BODIPY dyes, such as BODIPY 493/503, BODIPY FL, BODIPY R6G, BODIPY 530/550, BODIPY TMR, BODIPY 558/568, BODIPY 558/568, BODIPY 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY TR, BODIPY 630/650, BODIPY 650/665, Cascade Blue, Cascade Yellow, Dansyl, lissamine rhodamine B, Marina Blue, Oregon Green 488, Oregon Green 514, Pacific Blue, rhodamine 6G, rhodamine green, rhodamine red, tetramethylrhodamine, Texas Red (available from Molecular Probes, Inc., Eugene, OR, USA).

The polypeptides of the present invention can also be conjugated to fluorophores, other proteins, and other macromolecules, using bifunctional linking reagents. Common homobifunctional reagents include, *e.g.*, APG, AEDP, BASED, BMB, BMDB, BMH, BMOE, BM[PEO]3, BM[PEO]4, BS3, BSOCOES, DFDNB, DMA, DMP, DMS, DPDPB,

DSG, DSP (Lomant's Reagent), DSS, DST, DTBP, DTME, DTSSP, EGS, HBVS, Sulfo-BSOCOES, Sulfo-DST, Sulfo-EGS (all available from Pierce, Rockford, IL, USA); common heterobifunctional cross-linkers include ABH, AMAS, ANB-NOS, APDP, ASBA, BMPA, BMPH, BMPS, EDC, EMCA, EMCH, EMCS, KMUA, KMUH, GMBS, LC-SMCC, LC-SPDP, MBS, M2C2H, MPBH, MSA, NHS-ASA, PDPH, PMPI, SADP, SAED, SAND, SANPAH, SASD, SATP, SBAP, SFAD, SIA, SIAB, SMCC, SMPB, SMPH, SMPT, SPDP, Sulfo-EMCS, Sulfo-GMBS, Sulfo-HSAB, Sulfo-KMUS, Sulfo-LC-SPDP, Sulfo-MBS, Sulfo-NHS-LC-ASA, Sulfo-SADP, Sulfo-SANPAH, Sulfo-SIAB, Sulfo-SMCC, Sulfo-SMPB, Sulfo-LC-SMPT, SVSB, TFCS (all available
5
10 Pierce, Rockford, IL, USA).

Polypeptides of the present invention, including full length polypeptides, fragments and fusion proteins, can be conjugated, using such cross-linking reagents, to fluorophores that are not amine- or thiol-reactive. Other labels that usefully can be conjugated to polypeptides of the present invention include radioactive labels,
15 echosonographic contrast reagents, and MRI contrast agents.

Polypeptides of the present invention, including full length polypeptides, fragments and fusion proteins, can also usefully be conjugated using cross-linking agents to carrier proteins, such as KLH, bovine thyroglobulin, and even bovine serum albumin (BSA), to increase immunogenicity for raising anti-CSP antibodies.

20 Polypeptides of the present invention, including full length polypeptides, fragments and fusion proteins, can also usefully be conjugated to polyethylene glycol (PEG); PEGylation increases the serum half life of proteins administered intravenously for replacement therapy. Delgado *et al.*, *Crit. Rev. Ther. Drug Carrier Syst.* 9(3-4): 249-304 (1992); Scott *et al.*, *Curr. Pharm. Des.* 4(6): 423-38 (1998); DeSantis *et al.*, *Curr. Opin. Biotechnol.* 10(4): 324-30 (1999). PEG monomers can be attached to the protein directly
25 or through a linker, with PEGylation using PEG monomers activated with tresyl chloride (2,2,2-trifluoroethanesulphonyl chloride) permitting direct attachment under mild conditions.

Polypeptides of the present invention are also inclusive of analogs of a polypeptide
30 encoded by a nucleic acid molecule according to the instant invention. In a preferred embodiment, this polypeptide is a CSP. In a more preferred embodiment, this polypeptide is derived from a polypeptide having part or all of the amino acid sequence of SEQ ID NO: 95-248. Also preferred is an analog polypeptide comprising one or more

substitutions of non-natural amino acids or non-native inter-residue bonds compared to the naturally occurring polypeptide. In one embodiment, the analog is structurally similar to a CSP, but one or more peptide linkages is replaced by a linkage selected from the group consisting of --CH₂NH--, --CH₂S--, --CH₂-CH₂--, --CH=CH--(cis and trans), --COCH₂--,
5 --CH(OH)CH₂-- and --CH₂SO--. In another embodiment, the analog comprises substitution of one or more amino acids of a CSP with a D-amino acid of the same type or other non-natural amino acid in order to generate more stable peptides. D-amino acids can readily be incorporated during chemical peptide synthesis: peptides assembled from D-amino acids are more resistant to proteolytic attack; incorporation of D-amino acids can
10 also be used to confer specific three-dimensional conformations on the peptide. Other amino acid analogues commonly added during chemical synthesis include ornithine, norleucine, phosphorylated amino acids (typically phosphoserine, phosphothreonine, phosphotyrosine), L-malonyltyrosine, a non-hydrolyzable analog of phosphotyrosine (*see, e.g., Kole et al., Biochem. Biophys. Res. Com.* 209: 817-821 (1995)), and various
15 halogenated phenylalanine derivatives.

Non-natural amino acids can be incorporated during solid phase chemical synthesis or by recombinant techniques, although the former is typically more common. Solid phase chemical synthesis of peptides is well established in the art. Procedures are described, *inter alia*, in Chan *et al.* (eds.), Fmoc Solid Phase Peptide Synthesis: A
20 Practical Approach (Practical Approach Series), Oxford Univ. Press (March 2000); Jones, Amino Acid and Peptide Synthesis (Oxford Chemistry Primers, No 7), Oxford Univ. Press (1992); and Bodanszky, Principles of Peptide Synthesis (Springer Laboratory), Springer Verlag (1993).

Amino acid analogues having detectable labels are also usefully incorporated
25 during synthesis to provide derivatives and analogs. Biotin, for example can be added using biotinoyl-(9-fluorenylmethoxycarbonyl)-L-lysine (FMOC biocytin) (Molecular Probes, Eugene, OR, USA). Biotin can also be added enzymatically by incorporation into a fusion protein of an *E. coli* BirA substrate peptide. The FMOC and tBOC derivatives of dabcyL-L-lysine (Molecular Probes, Inc., Eugene, OR, USA) can be used to incorporate
30 the dabcyL chromophore at selected sites in the peptide sequence during synthesis. The aminonaphthalene derivative EDANS, the most common fluorophore for pairing with the dabcyL quencher in fluorescence resonance energy transfer (FRET) systems, can be

introduced during automated synthesis of peptides by using EDANS-FMOC-L-glutamic acid or the corresponding *t*BOC derivative (both from Molecular Probes, Inc., Eugene, OR, USA). Tetramethylrhodamine fluorophores can be incorporated during automated FMOC synthesis of peptides using (FMOC)-TMR-L-lysine (Molecular Probes, Inc.

5 Eugene, OR, USA).

Other useful amino acid analogues that can be incorporated during chemical synthesis include aspartic acid, glutamic acid, lysine, and tyrosine analogues having allyl side-chain protection (Applied Biosystems, Inc., Foster City, CA, USA); the allyl side chain permits synthesis of cyclic, branched-chain, sulfonated, glycosylated, and

10 phosphorylated peptides.

A large number of other FMOC-protected non-natural amino acid analogues capable of incorporation during chemical synthesis are available commercially, including, *e.g.*, Fmoc-2-aminobicyclo[2.2.1]heptane-2-carboxylic acid, Fmoc-3-endo-aminobicyclo[2.2.1]heptane-2-endo-carboxylic acid, Fmoc-3-exo-aminobicyclo[2.2.1]heptane-2-exo-carboxylic acid, Fmoc-3-endo-amino-bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid, Fmoc-3-exo-amino-bicyclo[2.2.1]hept-5-ene-2-exo-carboxylic acid, Fmoc-cis-2-amino-1-cyclohexanecarboxylic acid, Fmoc-trans-2-amino-1-cyclohexanecarboxylic acid, Fmoc-1-amino-1-cyclopentanecarboxylic acid, Fmoc-cis-2-amino-1-cyclopentanecarboxylic acid, Fmoc-1-amino-1-cyclopropanecarboxylic acid, Fmoc-D-2-amino-4-(ethylthio)butyric acid, Fmoc-L-2-amino-4-(ethylthio)butyric acid, Fmoc-L-buthionine, Fmoc-S-methyl-L-Cysteine, Fmoc-2-aminobenzoic acid (anthranillic acid), Fmoc-3-aminobenzoic acid, Fmoc-4-aminobenzoic acid, Fmoc-2-aminobenzophenone-2'-carboxylic acid, Fmoc-N-(4-aminobenzoyl)- β -alanine, Fmoc-2-amino-4,5-dimethoxybenzoic acid, Fmoc-4-aminohippuric acid, Fmoc-2-amino-3-hydroxybenzoic acid, Fmoc-2-amino-5-hydroxybenzoic acid, Fmoc-3-amino-4-hydroxybenzoic acid, Fmoc-4-amino-3-hydroxybenzoic acid, Fmoc-4-amino-2-hydroxybenzoic acid, Fmoc-5-amino-2-hydroxybenzoic acid, Fmoc-2-amino-3-methoxybenzoic acid, Fmoc-4-amino-3-methoxybenzoic acid, Fmoc-2-amino-3-methylbenzoic acid, Fmoc-2-amino-5-methylbenzoic acid, Fmoc-2-amino-6-methylbenzoic acid, Fmoc-3-amino-2-methylbenzoic acid, Fmoc-3-amino-4-methylbenzoic acid, Fmoc-4-amino-3-methylbenzoic acid, Fmoc-3-amino-2-naphtoic acid, Fmoc-D,L-3-amino-3-phenylpropionic acid, Fmoc-L-Methyl-dopa, Fmoc-2-amino-4,6-dimethyl-3-

pyridinecarboxylic acid, Fmoc-D,L-amino-2-thiophenacetic acid, Fmoc-4-(carboxymethyl)piperazine, Fmoc-4-carboxypiperazine, Fmoc-4-(carboxymethyl)homopiperazine, Fmoc-4-phenyl-4-piperidinecarboxylic acid, Fmoc-L-1,2,3,4-tetrahydronorharman-3-carboxylic acid, Fmoc-L-thiazolidine-4-carboxylic acid, all
5 available from The Peptide Laboratory (Richmond, CA, USA).

Non-natural residues can also be added biosynthetically by engineering a suppressor tRNA, typically one that recognizes the UAG stop codon, by chemical aminoacylation with the desired unnatural amino acid. Conventional site-directed mutagenesis is used to introduce the chosen stop codon UAG at the site of interest in the
10 protein gene. When the acylated suppressor tRNA and the mutant gene are combined in an *in vitro* transcription/translation system, the unnatural amino acid is incorporated in response to the UAG codon to give a protein containing that amino acid at the specified position. Liu *et al.*, *Proc. Natl Acad. Sci. USA* 96(9): 4780-5 (1999); Wang *et al.*, *Science* 292(5516): 498-500 (2001).

15 *Fusion Proteins*

Another aspect of the present invention relates to the fusion of a polypeptide of the present invention to heterologous polypeptides. In a preferred embodiment, the polypeptide of the present invention is a CSP. In a more preferred embodiment, the polypeptide of the present invention that is fused to a heterologous polypeptide which
20 comprises part or all of the amino acid sequence of SEQ ID NO: 95-248, or is a mutein, homologous polypeptide, analog or derivative thereof. In an even more preferred embodiment, the fusion protein is encoded by a nucleic acid molecule comprising all or part of the nucleic acid sequence of SEQ ID NO: 1-94, or comprises all or part of a nucleic acid sequence that selectively hybridizes or is homologous to a nucleic acid molecule
25 comprising a nucleic acid sequence of SEQ ID NO: 1-94.

The fusion proteins of the present invention will include at least one fragment of a polypeptide of the present invention, which fragment is at least 6, typically at least 8, often at least 15, and usefully at least 16, 17, 18, 19, or 20 amino acids long. The fragment of the polypeptide of the present to be included in the fusion can usefully be at least 25
30 amino acids long, at least 50 amino acids long, and can be at least 75, 100, or even 150 amino acids long. Fusions that include the entirety of a polypeptide of the present invention have particular utility.

The heterologous polypeptide included within the fusion protein of the present invention is at least 6 amino acids in length, often at least 8 amino acids in length, and preferably at least 15, 20, or 25 amino acids in length. Fusions that include larger polypeptides, such as the IgG Fc region, and even entire proteins (such as GFP
5 chromophore-containing proteins) are particularly useful.

As described above in the description of vectors and expression vectors of the present invention, which discussion is incorporated here by reference in its entirety, heterologous polypeptides to be included in the fusion proteins of the present invention can usefully include those designed to facilitate purification and/or visualization of
10 recombinantly-expressed proteins. *See, e.g.,* Ausubel, Chapter 16, (1992), *supra*. Although purification tags can also be incorporated into fusions that are chemically synthesized, chemical synthesis typically provides sufficient purity that further purification by HPLC suffices; however, visualization tags as above described retain their utility even when the protein is produced by chemical synthesis, and when so included
15 render the fusion proteins of the present invention useful as directly detectable markers of the presence of a polypeptide of the invention.

As also discussed above, heterologous polypeptides to be included in the fusion proteins of the present invention can usefully include those that facilitate secretion of recombinantly expressed proteins into the periplasmic space or extracellular milieu for
20 prokaryotic hosts or into the culture medium for eukaryotic cells through incorporation of secretion signals and/or leader sequences. For example, a His⁶ tagged protein can be purified on a Ni affinity column and a GST fusion protein can be purified on a glutathione affinity column. Similarly, a fusion protein comprising the Fc domain of IgG can be purified on a Protein A or Protein G column and a fusion protein comprising an epitope
25 tag such as myc can be purified using an immunoaffinity column containing an anti-c-myc antibody. It is preferable that the epitope tag be separated from the protein encoded by the essential gene by an enzymatic cleavage site that can be cleaved after purification. See also the discussion of nucleic acid molecules encoding fusion proteins that may be expressed on the surface of a cell.

30 Other useful fusion proteins of the present invention include those that permit use of the polypeptide of the present invention as bait in a yeast two-hybrid system. *See* Bartel *et al.* (eds.), The Yeast Two-Hybrid System, Oxford University Press (1997); Zhu *et al.*, Yeast Hybrid Technologies, Eaton Publishing (2000); Fields *et al.*, *Trends Genet.*

10(8): 286-92 (1994); Mendelsohn *et al.*, *Curr. Opin. Biotechnol.* 5(5): 482-6 (1994); Luban *et al.*, *Curr. Opin. Biotechnol.* 6(1): 59-64 (1995); Allen *et al.*, *Trends Biochem. Sci.* 20(12): 511-6 (1995); Drees, *Curr. Opin. Chem. Biol.* 3(1): 64-70 (1999); Topcu *et al.*, *Pharm. Res.* 17(9): 1049-55 (2000); Fashena *et al.*, *Gene* 250(1-2): 1-14 (2000); Colas
5 *et al.*, *Nature* 380, 548-550 (1996); Norman, T. *et al.*, *Science* 285, 591-595 (1999); Fabbri *et al.*, *Oncogene* 18, 4357-4363 (1999); Xu *et al.*, *Proc Natl Acad Sci U S A.* 94, 12473-12478 (1997); Yang, *et al.*, *Nuc. Acids Res.* 23, 1152-1156 (1995); Kolonin *et al.*, *Proc Natl Acad Sci U S A* 95, 14266-14271 (1998); Cohen *et al.*, *Proc Natl Acad Sci U S A* 95, 14272-14277 (1998); Uetz, *et al.* *Nature* 403, 623-627(2000); Ito, *et al.*, *Proc Natl*
10 *Acad Sci U S A* 98, 4569-4574 (2001). Typically, such fusion is to either *E. coli* LexA or yeast GAL4 DNA binding domains. Related bait plasmids are available that express the bait fused to a nuclear localization signal.

Other useful fusion proteins include those that permit display of the encoded polypeptide on the surface of a phage or cell, fusions to intrinsically fluorescent proteins,
15 such as green fluorescent protein (GFP), and fusions to the IgG Fc region, as described above.

The polypeptides of the present invention can also usefully be fused to protein toxins, such as *Pseudomonas* exotoxin A, diphtheria toxin, shiga toxin A, anthrax toxin lethal factor, or ricin, in order to effect ablation of cells that bind or take up the proteins of
20 the present invention.

Fusion partners include, *inter alia*, myc, hemagglutinin (HA), GST, immunoglobulins, β -galactosidase, biotin trpE, protein A, β -lactamase, α -amylase, maltose binding protein, alcohol dehydrogenase, polyhistidine (for example, six histidine at the amino and/or carboxyl terminus of the polypeptide), lacZ, green fluorescent protein
25 (GFP), yeast α mating factor, GAL4 transcription activation or DNA binding domain, luciferase, and serum proteins such as ovalbumin, albumin and the constant domain of IgG. See, e.g., Ausubel (1992), *supra* and Ausubel (1999), *supra*. Fusion proteins may also contain sites for specific enzymatic cleavage, such as a site that is recognized by enzymes such as Factor XIII, trypsin, pepsin, or any other enzyme known in the art.
30 Fusion proteins will typically be made by either recombinant nucleic acid methods, as described above, chemically synthesized using techniques well known in the art (e.g., a Merrifield synthesis), or produced by chemical cross-linking.

Another advantage of fusion proteins is that the epitope tag can be used to bind the fusion protein to a plate or column through an affinity linkage for screening binding proteins or other molecules that bind to the CSP.

As further described below, the polypeptides of the present invention can readily
5 be used as specific immunogens to raise antibodies that specifically recognize polypeptides of the present invention including CSPs and their allelic variants and homologues. The antibodies, in turn, can be used, *inter alia*, specifically to assay for the polypeptides of the present invention, particularly CSPs, *e.g.* by ELISA for detection of protein fluid samples, such as serum, by immunohistochemistry or laser scanning
10 cytometry, for detection of protein in tissue samples, or by flow cytometry, for detection of intracellular protein in cell suspensions, for specific antibody-mediated isolation and/or purification of CSPs, as for example by immunoprecipitation, and for use as specific agonists or antagonists of CSPs.

One may determine whether polypeptides of the present invention including CSPs,
15 muteins, homologous proteins or allelic variants or fusion proteins of the present invention are functional by methods known in the art. For instance, residues that are tolerant of change while retaining function can be identified by altering the polypeptide at known residues using methods known in the art, such as alanine scanning mutagenesis, Cunningham *et al.*, *Science* 244(4908): 1081-5 (1989); transposon linker scanning
20 mutagenesis, Chen *et al.*, *Gene* 263(1-2): 39-48 (2001); combinations of homolog- and alanine-scanning mutagenesis, Jin *et al.*, *J. Mol. Biol.* 226(3): 851-65 (1992); and combinatorial alanine scanning, Weiss *et al.*, *Proc. Natl. Acad. Sci USA* 97(16): 8950-4 (2000), followed by functional assay. Transposon linker scanning kits are available commercially (New England Biolabs, Beverly, MA, USA, catalog. no. E7-102S;
25 EZ::TN™ In-Frame Linker Insertion Kit, catalogue no. EZI04KN, (Epicentre Technologies Corporation, Madison, WI, USA).

Purification of the polypeptides or fusion proteins of the present invention is well known and within the skill of one having ordinary skill in the art. *See, e.g.*, Scopes, Protein Purification, 2d.ed. (1987). Purification of recombinantly expressed polypeptides
30 is described above. Purification of chemically-synthesized peptides can readily be effected, *e.g.*, by HPLC.

Accordingly, it is an aspect of the present invention to provide the isolated polypeptides or fusion proteins of the present invention in pure or substantially pure form

in the presence or absence of a stabilizing agent. Stabilizing agents include both proteinaceous and non-proteinaceous material and are well known in the art. Stabilizing agents, such as albumin and polyethylene glycol (PEG) are known and are commercially available.

5 Although high levels of purity are preferred when the isolated polypeptide or fusion protein of the present invention are used as therapeutic agents, such as in vaccines and replacement therapy, the isolated polypeptides of the present invention are also useful at lower purity. For example, partially purified polypeptides of the present invention can be used as immunogens to raise antibodies in laboratory animals.

10 In a preferred embodiment, the purified and substantially purified polypeptides of the present invention are in compositions that lack detectable ampholytes, acrylamide monomers, bis-acrylamide monomers, and polyacrylamide.

 The polypeptides or fusion proteins of the present invention can usefully be attached to a substrate. The substrate can be porous or solid, planar or non-planar; the
15 bond can be covalent or noncovalent. For example, the peptides of the invention may be stabilized by covalent linkage to albumin. See, U.S. Patent No. 5,876,969, the contents of which are hereby incorporated in its entirety.

 The polypeptides or fusion proteins of the present invention can also be usefully bound to a porous substrate, commonly a membrane, typically comprising nitrocellulose,
20 polyvinylidene fluoride (PVDF), or cationically derivatized, hydrophilic PVDF; so bound, the polypeptides or fusion proteins of the present invention can be used to detect and quantify antibodies, *e.g.* in serum, that bind specifically to the immobilized polypeptide or fusion protein of the present invention.

 As another example, the polypeptides or fusion proteins of the present invention
25 can usefully be bound to a substantially nonporous substrate, such as plastic, to detect and quantify antibodies, *e.g.* in serum, that bind specifically to the immobilized protein of the present invention. Such plastics include polymethylacrylic, polyethylene, polypropylene, polyacrylate, polymethylmethacrylate, polyvinylchloride, polytetrafluoroethylene, polystyrene, polycarbonate, polyacetal, polysulfone, celluloseacetate, cellulosenitrate,
30 nitrocellulose, or mixtures thereof; when the assay is performed in a standard microtiter dish, the plastic is typically polystyrene.

 The polypeptides and fusion proteins of the present invention can also be attached to a substrate suitable for use as a surface enhanced laser desorption ionization source; so

attached, the polypeptide or fusion protein of the present invention is useful for binding and then detecting secondary proteins that bind with sufficient affinity or avidity to the surface-bound polypeptide or fusion protein to indicate biologic interaction there between.

- 5 The polypeptides or fusion proteins of the present invention can also be attached to a substrate suitable for use in surface plasmon resonance detection; so attached, the polypeptide or fusion protein of the present invention is useful for binding and then detecting secondary proteins that bind with sufficient affinity or avidity to the surface-bound polypeptide or fusion protein to indicate biological interaction there between.

Alternative Transcripts

- 10 In another aspect, the present invention provides splice variants of genes and proteins encoded thereby. The identification of a novel splice variant which encodes an amino acid sequence with a novel region can be targeted for the generation of reagents for use in detection and/or treatment of cancer. The novel amino acid sequence may lead to a unique protein structure, protein subcellular localization, biochemical processing or
- 15 function of the splice variant. This information can be used to directly or indirectly facilitate the generation of additional or novel therapeutics or diagnostics. The nucleotide sequence in this novel splice variant can be used as a nucleic acid probe for the diagnosis and/or treatment of cancer.

- Specifically, the newly identified sequences may enable the production of new
- 20 antibodies or compounds directed against the novel region for use as a therapeutic or diagnostic. Alternatively, the newly identified sequences may alter the biochemical or biological properties of the encoded protein in such a way as to enable the generation of improved or different therapeutics targeting this protein.

Antibodies

- 25 In another aspect, the invention provides antibodies, including fragments and derivatives thereof, that bind specifically to polypeptides encoded by the nucleic acid molecules of the invention. In a preferred embodiment, the antibodies are specific for a polypeptide that is a CSP, or a fragment, mutein, derivative, analog or fusion protein thereof. In a more preferred embodiment, the antibodies are specific for a polypeptide that
- 30 comprises SEQ ID NO: 95-248, or a fragment, mutein, derivative, analog or fusion protein thereof.

The antibodies of the present invention can be specific for linear epitopes, discontinuous epitopes, or conformational epitopes of such proteins or protein fragments, either as present on the protein in its native conformation or, in some cases, as present on the proteins as denatured, as, *e.g.*, by solubilization in SDS. New epitopes may also be
5 due to a difference in post translational modifications (PTMs) in disease versus normal tissue. For example, a particular site on a CSP may be glycosylated in cancerous cells, but not glycosylated in normal cells or vice versa. In addition, alternative splice forms of a CSP may be indicative of cancer. Differential degradation of the C or N-terminus of a CSP may also be a marker or target for anticancer therapy. For example, a CSP may be
10 N-terminal degraded in cancer cells exposing new epitopes to antibodies which may selectively bind for diagnostic or therapeutic uses.

As is well known in the art, the degree to which an antibody can discriminate among molecular species in a mixture will depend, in part, upon the conformational relatedness of the species in the mixture; typically, the antibodies of the present invention
15 will discriminate over adventitious binding to non-CSP polypeptides by at least two-fold, more typically by at least 5-fold, typically by more than 10-fold, 25-fold, 50-fold, 75-fold, and often by more than 100-fold, and on occasion by more than 500-fold or 1000-fold. When used to detect the proteins or protein fragments of the present invention, the antibody of the present invention is sufficiently specific when it can be used to determine
20 the presence of the polypeptide of the present invention in samples derived from human colon.

Typically, the affinity or avidity of an antibody (or antibody multimer, as in the case of an IgM pentamer) of the present invention for a protein or protein fragment of the present invention will be at least about 1×10^{-6} molar (M), typically at least about 5×10^{-7}
25 M, 1×10^{-7} M, with affinities and avidities of at least 1×10^{-8} M, 5×10^{-9} M, 1×10^{-10} M and up to 1×10^{-13} M proving especially useful.

The antibodies of the present invention can be naturally occurring forms, such as IgG, IgM, IgD, IgE, IgY, and IgA, from any avian, reptilian, or mammalian species.

Human antibodies can, but will infrequently, be drawn directly from human donors
30 or human cells. In such case, antibodies to the polypeptides of the present invention will typically have resulted from fortuitous immunization, such as autoimmune immunization, with the polypeptide of the present invention. Such antibodies will typically, but will not

invariably, be polyclonal. In addition, individual polyclonal antibodies may be isolated and cloned to generate monoclonals.

Human antibodies are more frequently obtained using transgenic animals that express human immunoglobulin genes, which transgenic animals can be affirmatively immunized with the protein immunogen of the present invention. Human Ig-transgenic mice capable of producing human antibodies and methods of producing human antibodies therefrom upon specific immunization are described, *inter alia*, in U.S. Patent Nos. 6,162,963; 6,150,584; 6,114,598; 6,075,181; 5,939,598; 5,877,397; 5,874,299; 5,814,318; 5,789,650; 5,770,429; 5,661,016; 5,633,425; 5,625,126; 5,569,825; 5,545,807; 5,545,806, 10 and 5,591,669, the disclosures of which are incorporated herein by reference in their entireties. Such antibodies are typically monoclonal, and are typically produced using techniques developed for production of murine antibodies.

Human antibodies are particularly useful, and often preferred, when the antibodies of the present invention are to be administered to human beings as *in vivo* diagnostic or therapeutic agents, since recipient immune response to the administered antibody will 15 often be substantially less than that occasioned by administration of an antibody derived from another species, such as mouse.

IgG, IgM, IgD, IgE, IgY, and IgA antibodies of the present invention are also usefully obtained from other species, including mammals such as rodents (typically 20 mouse, but also rat, guinea pig, and hamster), lagomorphs (typically rabbits), and also larger mammals, such as sheep, goats, cows, and horses; or egg laying birds or reptiles such as chickens or alligators. In such cases, as with the transgenic human-antibody-producing non-human mammals, fortuitous immunization is not required, and the non-human mammal is typically affirmatively immunized, according to standard immunization 25 protocols, with the polypeptide of the present invention. One form of avian antibodies may be generated using techniques described in WO 00/29444, published 25 May 2000, which is herein incorporated by reference in its entirety.

As discussed above, virtually all fragments of 8 or more contiguous amino acids of a polypeptide of the present invention can be used effectively as immunogens when 30 conjugated to a carrier, typically a protein such as bovine thyroglobulin, keyhole limpet hemocyanin, or bovine serum albumin, conveniently using a bifunctional linker such as those described elsewhere above, which discussion is incorporated by reference here.

Immunogenicity can also be conferred by fusion of the polypeptides of the present invention to other moieties. For example, polypeptides of the present invention can be produced by solid phase synthesis on a branched polylysine core matrix; these multiple antigenic peptides (MAPs) provide high purity, increased avidity, accurate chemical
5 definition and improved safety in vaccine development. Tam *et al.*, *Proc. Natl. Acad. Sci. USA* 85: 5409-5413 (1988); Posnett *et al.*, *J. Biol. Chem.* 263: 1719-1725 (1988).

Protocols for immunizing non-human mammals or avian species are well-established in the art. See Harlow *et al.* (eds.), Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory (1998); Coligan *et al.* (eds.), Current Protocols in
10 Immunology, John Wiley & Sons, Inc. (2001); Zola, Monoclonal Antibodies: Preparation and Use of Monoclonal Antibodies and Engineered Antibody Derivatives (Basics: From Background to Bench), Springer Verlag (2000); Gross M, Speck *J.Dtsch. Tierarztl. Wochenschr.* 103: 417-422 (1996). Immunization protocols often include multiple immunizations, either with or without adjuvants such as Freund's complete adjuvant and
15 Freund's incomplete adjuvant, and may include naked DNA immunization. Moss, *Semin. Immunol.* 2: 317-327 (1990).

Antibodies from non-human mammals and avian species can be polyclonal or monoclonal, with polyclonal antibodies having certain advantages in immunohistochemical detection of the polypeptides of the present invention and
20 monoclonal antibodies having advantages in identifying and distinguishing particular epitopes of the polypeptides of the present invention. Antibodies from avian species may have particular advantage in detection of the polypeptides of the present invention, in human serum or tissues. Vikinge *et al.*, *Biosens. Bioelectron.* 13: 1257-1262 (1998). Following immunization, the antibodies of the present invention can be obtained using any
25 art-accepted technique. Such techniques are well known in the art and are described in detail in references such as Coligan, *supra*; Zola, *supra*; Howard *et al.* (eds.), Basic Methods in Antibody Production and Characterization, CRC Press (2000); Harlow, *supra*; Davis (ed.), Monoclonal Antibody Protocols, Vol. 45, Humana Press (1995); Delves (ed.), Antibody Production: Essential Techniques, John Wiley & Son Ltd (1997); and Kenney,
30 Antibody Solution: An Antibody Methods Manual, Chapman & Hall (1997).

Briefly, such techniques include, *inter alia*, production of monoclonal antibodies by hybridomas and expression of antibodies or fragments or derivatives thereof from host cells engineered to express immunoglobulin genes or fragments thereof. These two

methods of production are not mutually exclusive: genes encoding antibodies specific for the polypeptides of the present invention can be cloned from hybridomas and thereafter expressed in other host cells. Nor need the two necessarily be performed together: *e.g.*, genes encoding antibodies specific for the polypeptides of the present invention can be
5 cloned directly from B cells known to be specific for the desired protein, as further described in U.S. Patent No. 5,627,052, the disclosure of which is incorporated herein by reference in its entirety, or from antibody-displaying phage.

Recombinant expression in host cells is particularly useful when fragments or derivatives of the antibodies of the present invention are desired.

10 Host cells for recombinant antibody production of whole antibodies, antibody fragments, or antibody derivatives can be prokaryotic or eukaryotic.

Prokaryotic hosts are particularly useful for producing phage displayed antibodies of the present invention.

The technology of phage-displayed antibodies, in which antibody variable region
15 fragments are fused, for example, to the gene III protein (pIII) or gene VIII protein (pVIII) for display on the surface of filamentous phage, such as M13, is by now well-established. *See, e.g.*, Sidhu, *Curr. Opin. Biotechnol.* 11(6): 610-6 (2000); Griffiths *et al.*, *Curr. Opin. Biotechnol.* 9(1): 102-8 (1998); Hoogenboom *et al.*, *Immunotechnology*, 4(1): 1-20 (1998); Rader *et al.*, *Current Opinion in Biotechnology* 8: 503-508 (1997); Aujame *et al.*, *Human*
20 *Antibodies* 8: 155-168 (1997); Hoogenboom, *Trends in Biotechnol.* 15: 62-70 (1997); de Kruif *et al.*, 17: 453-455 (1996); Barbas *et al.*, *Trends in Biotechnol.* 14: 230-234 (1996); Winter *et al.*, *Ann. Rev. Immunol.* 433-455 (1994). Techniques and protocols required to generate, propagate, screen (pan), and use the antibody fragments from such libraries have recently been compiled. *See, e.g.*, Barbas (2001), *supra*; Kay, *supra*; and Abelson, *supra*.

25 Typically, phage-displayed antibody fragments are scFv fragments or Fab fragments; when desired, full length antibodies can be produced by cloning the variable regions from the displaying phage into a complete antibody and expressing the full length antibody in a further prokaryotic or a eukaryotic host cell. Eukaryotic cells are also useful for expression of the antibodies, antibody fragments, and antibody derivatives of the
30 present invention. For example, antibody fragments of the present invention can be produced in *Pichia pastoris* and in *Saccharomyces cerevisiae*. *See, e.g.*, Takahashi *et al.*, *Biosci. Biotechnol. Biochem.* 64(10): 2138-44 (2000); Freyre *et al.*, *J. Biotechnol.* 76(2-3):1 57-63 (2000); Fischer *et al.*, *Biotechnol. Appl. Biochem.* 30 (Pt 2): 117-20

(1999); Pennell *et al.*, *Res. Immunol.* 149(6): 599-603 (1998); Eldin *et al.*, *J. Immunol. Methods.* 201(1): 67-75 (1997);, Frenken *et al.*, *Res. Immunol.* 149(6): 589-99 (1998); and Shusta *et al.*, *Nature Biotechnol.* 16(8): 773-7 (1998).

Antibodies, including antibody fragments and derivatives, of the present invention
5 can also be produced in insect cells. See, e.g., Li *et al.*, *Protein Expr. Purif.* 21(1): 121-8 (2001); Ailor *et al.*, *Biotechnol. Bioeng.* 58(2-3): 196-203 (1998); Hsu *et al.*, *Biotechnol. Prog.* 13(1): 96-104 (1997); Edelman *et al.*, *Immunology* 91(1): 13-9 (1997); and Nesbit *et al.*, *J. Immunol. Methods* 151(1-2): 201-8 (1992).

Antibodies and fragments and derivatives thereof of the present invention can also
10 be produced in plant cells, particularly maize or tobacco, Giddings *et al.*, *Nature Biotechnol.* 18(11): 1151-5 (2000); Gavilondo *et al.*, *Biotechniques* 29(1): 128-38 (2000); Fischer *et al.*, *J. Biol. Regul. Homeost. Agents* 14(2): 83-92 (2000); Fischer *et al.*, *Biotechnol. Appl. Biochem.* 30 (Pt 2): 113-6 (1999); Fischer *et al.*, *Biol. Chem.* 380(7-8): 825-39 (1999); Russell, *Curr. Top. Microbiol. Immunol.* 240: 119-38 (1999); and Ma *et al.*, *Plant Physiol.* 109(2): 341-6 (1995).

Antibodies, including antibody fragments and derivatives, of the present invention can also be produced in transgenic, non-human, mammalian milk. See, e.g. Pollock *et al.*, *J. Immunol Methods.* 231: 147-57 (1999); Young *et al.*, *Res. Immunol.* 149: 609-10 (1998); and Limonta *et al.*, *Immunotechnology* 1: 107-13 (1995).

20 Mammalian cells useful for recombinant expression of antibodies, antibody fragments, and antibody derivatives of the present invention include CHO cells, COS cells, 293 cells, and myeloma cells. Verma *et al.*, *J. Immunol. Methods* 216(1-2):165-81 (1998) review and compare bacterial, yeast, insect and mammalian expression systems for expression of antibodies. Antibodies of the present invention can also be prepared by cell
25 free translation, as further described in Merk *et al.*, *J. Biochem. (Tokyo)* 125(2): 328-33 (1999) and Ryabova *et al.*, *Nature Biotechnol.* 15(1): 79-84 (1997), and in the milk of transgenic animals, as further described in Pollock *et al.*, *J. Immunol. Methods* 231(1-2): 147-57 (1999).

The invention further provides antibody fragments that bind specifically to one or
30 more of the polypeptides of the present invention or to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid

molecules of the present invention. Among such useful fragments are Fab, Fab', Fv, F(ab)'₂, and single chain Fv (scFv) fragments. Other useful fragments are described in Hudson, *Curr. Opin. Biotechnol.* 9(4): 395-402 (1998).

The present invention also relates to antibody derivatives that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention.

Among such useful derivatives are chimeric, primatized, and humanized antibodies; such derivatives are less immunogenic in human beings, and thus are more suitable for *in vivo* administration, than are unmodified antibodies from non-human mammalian species. Another useful method is PEGylation to increase the serum half life of the antibodies.

Chimeric antibodies typically include heavy and/or light chain variable regions (including both CDR and framework residues) of immunoglobulins of one species, typically mouse, fused to constant regions of another species, typically human. *See, e.g., Morrison et al., Proc. Natl. Acad. Sci USA* 81(21): 6851-5 (1984); Sharon *et al., Nature* 309(5966): 364-7 (1984); Takeda *et al., Nature* 314(6010): 452-4 (1985); and U.S. Patent No. 5,807,715 the disclosure of which is incorporated herein by reference in its entirety. Primatized and humanized antibodies typically include heavy and/or light chain CDRs from a murine antibody grafted into a non-human primate or human antibody V region framework, usually further comprising a human constant region, Riechmann *et al., Nature* 332(6162): 323-7 (1988); Co *et al., Nature* 351(6326): 501-2 (1991); and U.S. Patent Nos. 6,054,297; 5,821,337; 5,770,196; 5,766,886; 5,821,123; 5,869,619; 6,180,377; 6,013,256; 5,693,761; and 6,180,370, the disclosures of which are incorporated herein by reference in their entireties. Other useful antibody derivatives of the invention include heteromeric antibody complexes and antibody fusions, such as diabodies (bispecific antibodies), single-chain diabodies, and intrabodies.

It is contemplated that the nucleic acids encoding the antibodies of the present invention can be operably joined to other nucleic acids forming a recombinant vector for cloning or for expression of the antibodies of the invention. Accordingly, the present invention includes any recombinant vector containing the coding sequences, or part

thereof, whether for eukaryotic transduction, transfection or gene therapy. Such vectors may be prepared using conventional molecular biology techniques, known to those with skill in the art, and would comprise DNA encoding sequences for the immunoglobulin V-regions including framework and CDRs or parts thereof, and a suitable promoter either
5 with or without a signal sequence for intracellular transport. Such vectors may be transduced or transfected into eukaryotic cells or used for gene therapy (Marasco et al., *Proc. Natl. Acad. Sci. (USA)* 90: 7889-7893 (1993); Duan et al., *Proc. Natl. Acad. Sci. (USA)* 91: 5075-5079 (1994), by conventional techniques, known to those with skill in the art.

10 The antibodies of the present invention, including fragments and derivatives thereof, can usefully be labeled. It is, therefore, another aspect of the present invention to provide labeled antibodies that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited
15 by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention. The choice of label depends, in part, upon the desired use.

For example, when the antibodies of the present invention are used for immunohistochemical staining of tissue samples, the label can usefully be an enzyme that
20 catalyzes production and local deposition of a detectable product. Enzymes typically conjugated to antibodies to permit their immunohistochemical visualization are well known, and include alkaline phosphatase, β -galactosidase, glucose oxidase, horseradish peroxidase (HRP), and urease. Typical substrates for production and deposition of visually detectable products include o-nitrophenyl-beta-D-galactopyranoside (ONPG);
25 o-phenylenediamine dihydrochloride (OPD); p-nitrophenyl phosphate (PNPP); p-nitrophenyl-beta-D-galactopyranoside (PNPG); 3',3'-diaminobenzidine (DAB); 3-amino-9-ethylcarbazole (AEC); 4-chloro-1-naphthol (CN);
5-bromo-4-chloro-3-indolyl-phosphate (BCIP); ABTS®; BluoGal; iodonitrotetrazolium (INT); nitroblue tetrazolium chloride (NBT); phenazine methosulfate (PMS);
30 phenolphthalein monophosphate (PMP); tetramethyl benzidine (TMB); tetranitroblue tetrazolium (TNBT); X-Gal; X-Gluc; and X-Glucoside.

Other substrates can be used to produce products for local deposition that are luminescent. For example, in the presence of hydrogen peroxide (H_2O_2), horseradish

peroxidase (HRP) can catalyze the oxidation of cyclic diacylhydrazides, such as luminol. Immediately following the oxidation, the luminol is in an excited state (intermediate reaction product), which decays to the ground state by emitting light. Strong enhancement of the light emission is produced by enhancers, such as phenolic compounds. Advantages
5 include high sensitivity, high resolution, and rapid detection without radioactivity and requiring only small amounts of antibody. See, e.g., Thorpe *et al.*, *Methods Enzymol.* 133: 331-53 (1986); Kricka *et al.*, *J. Immunoassay* 17(1): 67-83 (1996); and Lundqvist *et al.*, *J. Biolumin. Chemilumin.* 10(6): 353-9 (1995). Kits for such enhanced chemiluminescent detection (ECL) are available commercially. The antibodies can also be labeled using
10 colloidal gold.

As another example, when the antibodies of the present invention are used, e.g., for flow cytometric detection, for scanning laser cytometric detection, or for fluorescent immunoassay, they can usefully be labeled with fluorophores. There are a wide variety of fluorophore labels that can usefully be attached to the antibodies of the present invention.
15 For flow cytometric applications, both for extracellular detection and for intracellular detection, common useful fluorophores can be fluorescein isothiocyanate (FITC), allophycocyanin (APC), R-phycoerythrin (PE), peridinin chlorophyll protein (PerCP), Texas Red, Cy3, Cy5, fluorescence resonance energy tandem fluorophores such as PerCP-Cy5.5, PE-Cy5, PE-Cy5.5, PE-Cy7, PE-Texas Red, and APC-Cy7.

20 Other fluorophores include, *inter alia*, Alexa Fluor® 350, Alexa Fluor® 488, Alexa Fluor® 532, Alexa Fluor® 546, Alexa Fluor® 568, Alexa Fluor® 594, Alexa Fluor® 647 (monoclonal antibody labeling kits available from Molecular Probes, Inc., Eugene, OR, USA), BODIPY dyes, such as BODIPY 493/503, BODIPY FL, BODIPY R6G, BODIPY 530/550, BODIPY TMR, BODIPY 558/568, BODIPY 558/568, BODIPY
25 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY TR, BODIPY 630/650, BODIPY 650/665, Cascade Blue, Cascade Yellow, Dansyl, lissamine rhodamine B, Marina Blue, Oregon Green 488, Oregon Green 514, Pacific Blue, rhodamine 6G, rhodamine green, rhodamine red, tetramethylrhodamine, Texas Red (available from Molecular Probes, Inc., Eugene, OR, USA), and Cy2, Cy3, Cy3.5, Cy5, Cy5.5, Cy7, all of
30 which are also useful for fluorescently labeling the antibodies of the present invention. For secondary detection using labeled avidin, streptavidin, captavidin or neutravidin, the antibodies of the present invention can usefully be labeled with biotin.

When the antibodies of the present invention are used, *e.g.*, for western blotting applications, they can usefully be labeled with radioisotopes, such as ^{33}P , ^{32}P , ^{35}S , ^3H , and ^{125}I . As another example, when the antibodies of the present invention are used for radioimmunotherapy, the label can usefully be ^{228}Th , ^{227}Ac , ^{225}Ac , ^{223}Ra , ^{213}Bi , ^{212}Pb , ^{212}Bi , ^{211}At , ^{203}Pb , ^{194}Os , ^{188}Re , ^{186}Re , ^{153}Sm , ^{149}Tb , ^{131}I , ^{125}I , ^{111}In , ^{105}Rh , $^{99\text{m}}\text{Tc}$, ^{97}Ru , ^{90}Y , ^{90}Sr , ^{88}Y , ^{72}Se , ^{67}Cu , or ^{47}Sc .

As another example, when the antibodies of the present invention are to be used for *in vivo* diagnostic use, they can be rendered detectable by conjugation to MRI contrast agents, such as gadolinium diethylenetriaminepentaacetic acid (DTPA), Lauffer *et al.*, *Radiology* 207(2): 529-38 (1998), or by radioisotopic labeling.

As would be understood, use of the labels described above is not restricted to the application as for which they were mentioned.

The antibodies of the present invention, including fragments and derivatives thereof, can also be conjugated to toxins, in order to target the toxin's ablative action to cells that display and/or express the polypeptides of the present invention. Commonly, the antibody in such immunotoxins is conjugated to *Pseudomonas* exotoxin A, diphtheria toxin, shiga toxin A, anthrax toxin lethal factor, or ricin. See Hall (ed.), Immunotoxin Methods and Protocols (Methods in Molecular Biology, vol. 166), Humana Press (2000); and Frankel *et al.* (eds.), Clinical Applications of Immunotoxins, Springer-Verlag (1998).

The antibodies of the present invention can usefully be attached to a substrate, and it is, therefore, another aspect of the invention to provide antibodies that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, attached to a substrate. Substrates can be porous or nonporous, planar or nonplanar. For example, the antibodies of the present invention can usefully be conjugated to filtration media, such as NHS-activated Sepharose or CNBr-activated Sepharose for purposes of immunoaffinity chromatography. For example, the antibodies of the present invention can usefully be attached to paramagnetic microspheres, typically by biotin-streptavidin interaction, which microsphere can then be used for isolation of cells that express or display the polypeptides of the present invention. As

another example, the antibodies of the present invention can usefully be attached to the surface of a microtiter plate for ELISA.

As noted above, the antibodies of the present invention can be produced in prokaryotic and eukaryotic cells. It is, therefore, another aspect of the present invention to
5 provide cells that express the antibodies of the present invention, including hybridoma cells, B cells, plasma cells, and host cells recombinantly modified to express the antibodies of the present invention.

In yet a further aspect, the present invention provides aptamers evolved to bind specifically to one or more of the CSPs of the present invention or to polypeptides
10 encoded by the CSNAs of the invention.

In sum, one of skill in the art, provided with the teachings of this invention, has available a variety of methods which may be used to alter the biological properties of the antibodies of this invention including methods which would increase or decrease the stability or half-life, immunogenicity, toxicity, affinity or yield of a given antibody
15 molecule, or to alter it in any other way that may render it more suitable for a particular application.

Transgenic Animals and Cells

In another aspect, the invention provides transgenic cells and non-human organisms comprising nucleic acid molecules of the invention. In a preferred
20 embodiment, the transgenic cells and non-human organisms comprise a nucleic acid molecule encoding a CSP. In a preferred embodiment, the CSP comprises an amino acid sequence selected from SEQ ID NO: 95-248, or a fragment, mutein, homologous protein or allelic variant thereof. In another preferred embodiment, the transgenic cells and non-human organism comprise a CSNA of the invention, preferably a CSNA comprising a
25 nucleotide sequence selected from the group consisting of SEQ ID NO: 1-94, or a part, substantially similar nucleic acid molecule, allelic variant or hybridizing nucleic acid molecule thereof.

In another embodiment, the transgenic cells and non-human organisms have a targeted disruption or replacement of the endogenous orthologue of the human CSG. The
30 transgenic cells can be embryonic stem cells or somatic cells. The transgenic non-human organisms can be chimeric, nonchimeric heterozygotes, and nonchimeric homozygotes. Methods of producing transgenic animals are well known in the art. *See, e.g., Hogan et*

al., Manipulating the Mouse Embryo: A Laboratory Manual, 2d ed., Cold Spring Harbor Press (1999); Jackson *et al.*, Mouse Genetics and Transgenics: A Practical Approach, Oxford University Press (2000); and Pinkert, Transgenic Animal Technology: A Laboratory Handbook, Academic Press (1999).

5 Any technique known in the art may be used to introduce a nucleic acid molecule of the invention into an animal to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection. (*see, e.g.*, Paterson *et al.*, *Appl. Microbiol. Biotechnol.* 40: 691-698 (1994); Carver *et al.*, *Biotechnology* 11: 1263-1270 (1993); Wright *et al.*, *Biotechnology* 9: 830-834 (1991); and U.S. Patent No. 10 4,873,191, herein incorporated by reference in its entirety); retrovirus-mediated gene transfer into germ lines, blastocysts or embryos (*see, e.g.*, Van der Putten *et al.*, *Proc. Natl. Acad. Sci., USA* 82: 6148-6152 (1985)); gene targeting in embryonic stem cells (*see, e.g.*, Thompson *et al.*, *Cell* 56: 313-321 (1989)); electroporation of cells or embryos (*see, e.g.*, Lo, 1983, *Mol. Cell. Biol.* 3: 1803-1814 (1983)); introduction using a gene gun (*see, e.g.*, Ulmer *et al.*, *Science* 259: 1745-49 (1993); introducing nucleic acid constructs into 15 embryonic pluripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (*see, e.g.*, Lavitrano *et al.*, *Cell* 57: 717-723 (1989)).

Other techniques include, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (*see, e.g.*, 20 Campell *et al.*, *Nature* 380: 64-66 (1996); Wilmut *et al.*, *Nature* 385: 810-813 (1997)). The present invention provides for transgenic animals that carry the transgene (*i.e.*, a nucleic acid molecule of the invention) in all their cells, as well as animals which carry the transgene in some, but not all their cells, *i.e.* *e.*, mosaic animals or chimeric animals.

The transgene may be integrated as a single transgene or as multiple copies, such 25 as in concatamers, *e. g.*, head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, *e.g.*, the teaching of Lasko *et al. et al.*, *Proc. Natl. Acad. Sci. USA* 89: 6232- 6236 (1992). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

30 Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the

transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse transcriptase-PCR (RT-PCR). Samples of transgenic gene-expressing tissue may also be evaluated

- 5 immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than
10 one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA
15 analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of
20 the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Methods for creating a transgenic animal with a disruption of a targeted gene are also well known in the art. In general, a vector is designed to comprise some nucleotide
25 sequences homologous to the endogenous targeted gene. The vector is introduced into a cell so that it may integrate, via homologous recombination with chromosomal sequences, into the endogenous gene, thereby disrupting the function of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type. *See, e.g., Gu et al., Science* 265: 103-106
30 (1994). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. *See, e.g., Smithies et al., Nature* 317: 230-234 (1985); Thomas et al., *Cell* 51: 503-512 (1987); Thompson et al., *Cell* 5: 313-321 (1989).

In one embodiment, a mutant, non-functional nucleic acid molecule of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous nucleic acid sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable
5 marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications
10 to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene. *See, e.g.,* Thomas, *supra* and Thompson, *supra*. However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

15 In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (*e.g.*, knockouts) are administered to a patient in vivo. Such cells may be obtained from an animal or patient or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells,
20 blood cells (*e.g.*, lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, *e.g.*, by transduction (using viral vectors, and preferably
25 vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc.

The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve
30 expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, *e.g.*, in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, *e.g.*, genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. *See, e.g.*, U.S. Patent Nos. 5,399,349 and 5,460,959, each of which is
5 incorporated by reference herein in its entirety.

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of
10 components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with
15 aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Computer Readable Means

A further aspect of the invention is a computer readable means for storing the nucleic acid and amino acid sequences of the instant invention. In a preferred
20 embodiment, the invention provides a computer readable means for storing SEQ ID NO: 95-248 and SEQ ID NO: 1-94 as described herein, as the complete set of sequences or in any combination. The records of the computer readable means can be accessed for reading and display and for interface with a computer system for the application of programs allowing for the location of data upon a query for data meeting certain criteria,
25 the comparison of sequences, the alignment or ordering of sequences meeting a set of criteria, and the like.

The nucleic acid and amino acid sequences of the invention are particularly useful as components in databases useful for search analyses as well as in sequence analysis algorithms. As used herein, the terms "nucleic acid sequences of the invention" and
30 "amino acid sequences of the invention" mean any detectable chemical or physical characteristic of a polynucleotide or polypeptide of the invention that is or may be reduced to or stored in a computer readable form. These include, without limitation,

chromatographic scan data or peak data, photographic data or scan data therefrom, and mass spectrographic data.

This invention provides computer readable media having stored thereon sequences of the invention. A computer readable medium may comprise one or more of the

5 following: a nucleic acid sequence comprising a sequence of a nucleic acid sequence of the invention; an amino acid sequence comprising an amino acid sequence of the invention; a set of nucleic acid sequences wherein at least one of said sequences comprises the sequence of a nucleic acid sequence of the invention; a set of amino acid sequences wherein at least one of said sequences comprises the sequence of an amino acid sequence

10 of the invention; a data set representing a nucleic acid sequence comprising the sequence of one or more nucleic acid sequences of the invention; a data set representing a nucleic acid sequence encoding an amino acid sequence comprising the sequence of an amino acid sequence of the invention; a set of nucleic acid sequences wherein at least one of said sequences comprises the sequence of a nucleic acid sequence of the invention; a set of

15 amino acid sequences wherein at least one of said sequences comprises the sequence of an amino acid sequence of the invention; a data set representing a nucleic acid sequence comprising the sequence of a nucleic acid sequence of the invention; a data set representing a nucleic acid sequence encoding an amino acid sequence comprising the sequence of an amino acid sequence of the invention. The computer readable medium can

20 be any composition of matter used to store information or data, including, for example, commercially available floppy disks, tapes, hard drives, compact disks, and video disks.

Also provided by the invention are methods for the analysis of character sequences, particularly genetic sequences. Preferred methods of sequence analysis include, for example, methods of sequence homology analysis, such as identity and

25 similarity analysis, RNA structure analysis, sequence assembly, cladistic analysis, sequence motif analysis, open reading frame determination, nucleic acid base calling, and sequencing chromatogram peak analysis.

A computer-based method is provided for performing nucleic acid sequence identity or similarity identification. This method comprises the steps of providing a

30 nucleic acid sequence comprising the sequence of a nucleic acid of the invention in a computer readable medium; and comparing said nucleic acid sequence to at least one nucleic acid or amino acid sequence to identify sequence identity or similarity.

A computer-based method is also provided for performing amino acid homology identification, said method comprising the steps of: providing an amino acid sequence comprising the sequence of an amino acid of the invention in a computer readable medium; and comparing said amino acid sequence to at least one nucleic acid or an amino acid sequence to identify homology.

A computer-based method is still further provided for assembly of overlapping nucleic acid sequences into a single nucleic acid sequence, said method comprising the steps of: providing a first nucleic acid sequence comprising the sequence of a nucleic acid of the invention in a computer readable medium; and screening for at least one overlapping region between said first nucleic acid sequence and a second nucleic acid sequence. In addition, the invention includes a method of using patterns of expression associated with either the nucleic acids or proteins in a computer-based method to diagnose disease.

Diagnostic Methods for Colon Cancer

The present invention also relates to quantitative and qualitative diagnostic assays and methods for detecting, diagnosing, monitoring, staging and predicting cancers by comparing expression of a CSNA or a CSP in a human patient that has or may have colon cancer, or who is at risk of developing colon cancer, with the expression of a CSNA or a CSP in a normal human control. For purposes of the present invention, "expression of a CSNA" or "CSNA expression" means the quantity of CSNA mRNA that can be measured by any method known in the art or the level of transcription that can be measured by any method known in the art in a cell, tissue, organ or whole patient. Similarly, the term "expression of a CSP" or "CSP expression" means the amount of CSP that can be measured by any method known in the art or the level of translation of a CSNA that can be measured by any method known in the art.

The present invention provides methods for diagnosing colon cancer in a patient, in particular adenocarcinoma, by analyzing for changes in levels of CSNA or CSP in cells, tissues, organs or bodily fluids compared with levels of CSNA or CSP in cells, tissues, organs or bodily fluids of preferably the same type from a normal human control, wherein an increase, or decrease in certain cases, in levels of a CSNA or CSP in the patient versus the normal human control is associated with the presence of colon cancer or with a predilection to the disease. In another preferred embodiment, the present invention

provides methods for diagnosing colon cancer in a patient by analyzing changes in the structure of the mRNA of a CSG compared to the mRNA from a normal control. These changes include, without limitation, aberrant splicing, alterations in polyadenylation and/or alterations in 5' nucleotide capping. In yet another preferred embodiment, the present invention provides methods for diagnosing colon cancer in a patient by analyzing changes in a CSP compared to a CSP from a normal patient. These changes include, *e.g.*, alterations, including post translational modifications such as glycosylation and/or phosphorylation of the CSP or changes in the subcellular CSP localization.

For purposes of the present invention, diagnosing means that CSNA or CSP levels are used to determine the presence or absence of disease in a patient. As will be understood by those of skill in the art, measurement of other diagnostic parameters may be required for definitive diagnosis or determination of the appropriate treatment for the disease. The determination may be made by a clinician, a doctor, a testing laboratory, or a patient using an over the counter test. The patient may have symptoms of disease or may be asymptomatic. In addition, the CSNA or CSP levels of the present invention may be used as screening marker to determine whether further tests or biopsies are warranted. In addition, the CSNA or CSP levels may be used to determine the vulnerability or susceptibility to disease.

In a preferred embodiment, the expression of a CSNA is measured by determining the amount of a mRNA that encodes an amino acid sequence selected from SEQ ID NO: 95-248, a homolog, an allelic variant, or a fragment thereof. In a more preferred embodiment, the CSNA expression that is measured is the level of expression of a CSNA mRNA selected from SEQ ID NO: 1-94, or a hybridizing nucleic acid, homologous nucleic acid or allelic variant thereof, or a part of any of these nucleic acid molecules. CSNA expression may be measured by any method known in the art, such as those described *supra*, including measuring mRNA expression by Northern blot, quantitative or qualitative reverse transcriptase PCR (RT-PCR), microarray, dot or slot blots or *in situ* hybridization. See, *e.g.*, Ausubel (1992), *supra*; Ausubel (1999), *supra*; Sambrook (1989), *supra*; and Sambrook (2001), *supra*. CSNA transcription may be measured by any method known in the art including using a reporter gene hooked up to the promoter of a CSG of interest or doing nuclear run-off assays. Alterations in mRNA structure, *e.g.*, aberrant splicing variants, may be determined by any method known in the art, including, RT-PCR followed by sequencing or restriction analysis. As necessary, CSNA expression

may be compared to a known control, such as normal colon nucleic acid, to detect a change in expression.

In another preferred embodiment, the expression of a CSP is measured by determining the level of a CSP having an amino acid sequence selected from the group consisting of SEQ ID NO: 95-248, a homolog, an allelic variant, or a fragment thereof. Such levels are preferably determined in at least one of cells, tissues, organs and/or bodily fluids, including determination of normal and abnormal levels. Thus, for instance, a diagnostic assay in accordance with the invention for diagnosing over- or underexpression of a CSNA or CSP compared to normal control bodily fluids, cells, or tissue samples may be used to diagnose the presence of colon cancer. The expression level of a CSP may be determined by any method known in the art, such as those described *supra*. In a preferred embodiment, the CSP expression level may be determined by radioimmunoassays, competitive-binding assays, ELISA, Western blot, FACS, immunohistochemistry, immunoprecipitation, proteomic approaches: two-dimensional gel electrophoresis (2D electrophoresis) and non-gel-based approaches such as mass spectrometry or protein interaction profiling. See, e.g., Harlow (1999), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), *supra*. Alterations in the CSP structure may be determined by any method known in the art, including, e.g., using antibodies that specifically recognize phosphoserine, phosphothreonine or phosphotyrosine residues, two-dimensional polyacrylamide gel electrophoresis (2D PAGE) and/or chemical analysis of amino acid residues of the protein. *Id.*

In a preferred embodiment, a radioimmunoassay (RIA) or an ELISA is used. An antibody specific to a CSP is prepared if one is not already available. In a preferred embodiment, the antibody is a monoclonal antibody. The anti-CSP antibody is bound to a solid support and any free protein binding sites on the solid support are blocked with a protein such as bovine serum albumin. A sample of interest is incubated with the antibody on the solid support under conditions in which the CSP will bind to the anti-CSP antibody. The sample is removed, the solid support is washed to remove unbound material, and an anti-CSP antibody that is linked to a detectable reagent (a radioactive substance for RIA and an enzyme for ELISA) is added to the solid support and incubated under conditions in which binding of the CSP to the labeled antibody will occur. After binding, the unbound labeled antibody is removed by washing. For an ELISA, one or more substrates are added to produce a colored reaction product that is based upon the amount of a CSP in the

sample. For an RIA, the solid support is counted for radioactive decay signals by any method known in the art. Quantitative results for both RIA and ELISA typically are obtained by reference to a standard curve.

Other methods to measure CSP levels are known in the art. For instance, a
5 competition assay may be employed wherein an anti-CSP antibody is attached to a solid support and an allocated amount of a labeled CSP and a sample of interest are incubated with the solid support. The amount of labeled CSP attached to the solid support can be correlated to the quantity of a CSP in the sample.

Of the proteomic approaches, 2D PAGE is a well known technique. Isolation of
10 individual proteins from a sample such as serum is accomplished using sequential separation of proteins by isoelectric point and molecular weight. Typically, polypeptides are first separated by isoelectric point (the first dimension) and then separated by size using an electric current (the second dimension). In general, the second dimension is perpendicular to the first dimension. Because no two proteins with different sequences are
15 identical on the basis of both size and charge, the result of 2D PAGE is a roughly square gel in which each protein occupies a unique spot. Analysis of the spots with chemical or antibody probes, or subsequent protein microsequencing can reveal the relative abundance of a given protein and the identity of the proteins in the sample.

Expression levels of a CSNA can be determined by any method known in the art,
20 including PCR and other nucleic acid methods, such as ligase chain reaction (LCR) and nucleic acid sequence based amplification (NASBA), can be used to detect malignant cells for diagnosis and monitoring of various malignancies. For example, reverse-transcriptase PCR (RT-PCR) is a powerful technique which can be used to detect the presence of a specific mRNA population in a complex mixture of thousands of other mRNA species. In
25 RT-PCR, an mRNA species is first reverse transcribed to complementary DNA (cDNA) with use of the enzyme reverse transcriptase; the cDNA is then amplified as in a standard PCR reaction.

Hybridization to specific DNA molecules (*e.g.*, oligonucleotides) arrayed on a solid support can be used to both detect the expression of and quantitate the level of
30 expression of one or more CSNAs of interest. In this approach, all or a portion of one or more CSNAs is fixed to a substrate. A sample of interest, which may comprise RNA, *e.g.*, total RNA or polyA-selected mRNA, or a complementary DNA (cDNA) copy of the RNA is incubated with the solid support under conditions in which hybridization will occur

between the DNA on the solid support and the nucleic acid molecules in the sample of interest. Hybridization between the substrate-bound DNA and the nucleic acid molecules in the sample can be detected and quantitated by several means, including, without limitation, radioactive labeling or fluorescent labeling of the nucleic acid molecule or a
5 secondary molecule designed to detect the hybrid.

The above tests can be carried out on samples derived from a variety of cells, bodily fluids and/or tissue extracts such as homogenates or solubilized tissue obtained from a patient. Tissue extracts are obtained routinely from tissue biopsy and autopsy material. Bodily fluids useful in the present invention include blood, urine, saliva or any
10 other bodily secretion or derivative thereof. As used herein "blood" includes whole blood, plasma, serum, circulating epithelial cells, constituents, or any derivative of blood.

In addition to detection in bodily fluids, the proteins and nucleic acids of the invention are suitable to detection by cell capture technology. Whole cells may be captured by a variety of methods for example magnetic separation, such as described in U.S.
15 Patent Nos. 5,200,084; 5,186,827; 5,108,933; and 4,925,788, the disclosures of which are incorporated herein by reference in their entireties. Epithelial cells may be captured using such products as Dynabeads® or CELlection™ (DynaL Biotech, Oslo, Norway). Alternatively, fractions of blood may be captured, e.g., the buffy coat fraction (50mm cells isolated from 5ml of blood) containing epithelial cells. In addition, cancer cells may be
20 captured using the techniques described in WO 00/47998, the disclosure of which is incorporated herein by reference in its entirety. Once the cells are captured or concentrated, the proteins or nucleic acids are detected by the means described in the subject application. Alternatively, nucleic acids may be captured directly from blood samples, see U.S. Patent Nos. 6,156,504, 5,501,963; or WO 01/42504, the disclosures of
25 which are incorporated herein by reference in their entireties.

In a preferred embodiment, the specimen tested for expression of CSNA or CSP includes without limitation colon tissue, fecal samples, colonocytes, colon cells grown in cell culture, blood, serum, lymph node tissue, and lymphatic fluid. In another preferred embodiment, especially when metastasis of a primary colon cancer is known or suspected,
30 specimens include, without limitation, tissues from brain, bone, bone marrow, liver, lungs, and adrenal glands. In general, the tissues may be sampled by biopsy, including, without limitation, needle biopsy, e.g., transthoracic needle aspiration, cervical mediastinoscopy,

endoscopic lymph node biopsy, video-assisted thoracoscopy, exploratory thoracotomy, bone marrow biopsy and bone marrow aspiration.

Colonocytes represent an important source of the CSP or CSNA because they provide a picture of the immediate past metabolic history of the GI tract of a subject. In addition, such cells are representative of the cell population from a statistically large sampling frame reflecting the state of the colonic mucosa along the entire length of the colon in a non-invasive manner, in contrast to a limited sampling by colonic biopsy using an invasive procedure involving endoscopy. Specific examples of patents describing the isolation of colonocytes include U.S. Patent Nos. 6,335,193; 6,020,137 5,741,650; 10 6,258,541; US 2001 0026925 A1; WO 00/63358 A1, the disclosures of which are incorporated herein by reference in their entireties.

All the methods of the present invention may optionally include determining the expression levels of one or more other cancer markers in addition to determining the expression level of a CSNA or CSP. In many cases, the use of another cancer marker will decrease the likelihood of false positives or false negatives. In one embodiment, the one 15 or more other cancer markers include other CSNA or CSPs as disclosed herein. Other cancer markers useful in the present invention will depend on the cancer being tested and are known to those of skill in the art. In a preferred embodiment, at least one other cancer marker in addition to a particular CSNA or CSP is measured. In a more preferred 20 embodiment, at least two other additional cancer markers are used. In an even more preferred embodiment, at least three, more preferably at least five, even more preferably at least ten additional cancer markers are used.

Diagnosing

In one aspect, the invention provides a method for determining the expression 25 levels and/or structural alterations of one or more CSNA and/or CSP in a sample from a patient suspected of having colon cancer. In general, the method comprises the steps of obtaining the sample from the patient, determining the expression level or structural alterations of a CSNA and/or CSP and then ascertaining whether the patient has colon cancer from the expression level of the CSNA or CSP. In general, if high expression 30 relative to a control of a CSNA or CSP is indicative of colon cancer, a diagnostic assay is considered positive if the level of expression of the CSNA or CSP is at least one and a half times higher, and more preferably are at least two times higher, still more preferably five

times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of a CSNA or CSP is indicative of colon cancer, a diagnostic assay is considered positive if the level of expression of the CSNA or CSP is at least one and a half
5 times lower, and more preferably are at least two times lower, still more preferably five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human control. The normal human control may be from a different patient or from uninvolved tissue of the same patient.

The present invention also provides a method of determining whether colon cancer
10 has metastasized in a patient. One may identify whether the colon cancer has metastasized by measuring the expression levels and/or structural alterations of one or more CSNAs and/or CSPs in a variety of tissues. The presence of a CSNA or CSP in a tissue other than colon at levels higher than that of corresponding noncancerous tissue (*e.g.*, the same tissue from another individual) is indicative of metastasis if high level expression of a CSNA or
15 CSP is associated with colon cancer. Similarly, the presence of a CSNA or CSP in a tissue other than colon at levels lower than that of corresponding noncancerous tissue is indicative of metastasis if low level expression of a CSNA or CSP is associated with colon cancer. Further, the presence of a structurally altered CSNA or CSP that is associated with colon cancer is also indicative of metastasis.

20 In general, if high expression relative to a control of a CSNA or CSP is indicative of metastasis, an assay for metastasis is considered positive if the level of expression of the CSNA or CSP is at least one and a half times higher, and more preferably are at least two times higher, still more preferably five times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human
25 control. In contrast, if low expression relative to a control of a CSNA or CSP is indicative of metastasis, an assay for metastasis is considered positive if the level of expression of the CSNA or CSP is at least one and a half times lower, and more preferably are at least two times lower, still more preferably five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human
30 control.

Staging

The invention also provides a method of staging colon cancer in a human patient. The method comprises identifying a human patient having colon cancer and analyzing cells, tissues or bodily fluids from such human patient for expression levels and/or structural alterations of one or more CSNAs or CSPs. First, one or more tumors from a variety of patients are staged according to procedures well known in the art, and the expression levels of one or more CSNAs or CSPs is determined for each stage to obtain a standard expression level for each CSNA and CSP. Then, the CSNA or CSP expression levels of the CSNA or CSP are determined in a biological sample from a patient whose stage of cancer is not known. The CSNA or CSP expression levels from the patient are then compared to the standard expression level. By comparing the expression level of the CSNAs and CSPs from the patient to the standard expression levels, one may determine the stage of the tumor. The same procedure may be followed using structural alterations of a CSNA or CSP to determine the stage of a colon cancer.

Monitoring

Further provided is a method of monitoring colon cancer in a human patient. One may monitor a human patient to determine whether there has been metastasis and, if there has been, when metastasis began to occur. One may also monitor a human patient to determine whether a preneoplastic lesion has become cancerous. One may also monitor a human patient to determine whether a therapy, *e.g.*, chemotherapy, radiotherapy or surgery, has decreased or eliminated the colon cancer. The monitoring may determine if there has been a reoccurrence and, if so, determine its nature. The method comprises identifying a human patient that one wants to monitor for colon cancer, periodically analyzing cells, tissues or bodily fluids from such human patient for expression levels of one or more CSNAs or CSPs, and comparing the CSNA or CSP levels over time to those CSNA or CSP expression levels obtained previously. Patients may also be monitored by measuring one or more structural alterations in a CSNA or CSP that are associated with colon cancer.

If increased expression of a CSNA or CSP is associated with metastasis, treatment failure, or conversion of a preneoplastic lesion to a cancerous lesion, then detecting an increase in the expression level of a CSNA or CSP indicates that the tumor is metastasizing, that treatment has failed or that the lesion is cancerous, respectively. One having ordinary skill in the art would recognize that if this were the case, then a decreased

expression level would be indicative of no metastasis, effective therapy or failure to progress to a neoplastic lesion. If decreased expression of a CSNA or CSP is associated with metastasis, treatment failure, or conversion of a preneoplastic lesion to a cancerous lesion, then detecting a decrease in the expression level of a CSNA or CSP indicates that
5 the tumor is metastasizing, that treatment has failed or that the lesion is cancerous, respectively. In a preferred embodiment, the levels of CSNAs or CSPs are determined from the same cell type, tissue or bodily fluid as prior patient samples. Monitoring a patient for onset of colon cancer metastasis is periodic and preferably is done on a quarterly basis, but may be done more or less frequently.

10 The methods described herein can further be utilized as prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with increased or decreased expression levels of a CSNA and/or CSP. The present invention provides a method in which a test sample is obtained from a human patient and one or more CSNAs and/or CSPs are detected. The presence of higher (or lower) CSNA or CSP
15 levels as compared to normal human controls is diagnostic for the human patient being at risk for developing cancer, particularly colon cancer. The effectiveness of therapeutic agents to decrease (or increase) expression or activity of one or more CSNAs and/or CSPs of the invention can also be monitored by analyzing levels of expression of the CSNAs and/or CSPs in a human patient in clinical trials or in *in vitro* screening assays such as in
20 human cells. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the human patient or cells, as the case may be, to the agent being tested.

Detection of Genetic Lesions or Mutations

The methods of the present invention can also be used to detect genetic lesions or
25 mutations in a CSG, thereby determining if a human with the genetic lesion is susceptible to developing colon cancer or to determine what genetic lesions are responsible, or are partly responsible, for a person's existing colon cancer. Genetic lesions can be detected, for example, by ascertaining the existence of a deletion, insertion and/or substitution of one or more nucleotides from the CSGs of this invention, a chromosomal rearrangement
30 of a CSG, an aberrant modification of a CSG (such as of the methylation pattern of the genomic DNA), or allelic loss of a CSG. Methods to detect such lesions in the CSG of

this invention are known to those having ordinary skill in the art following the teachings of the specification.

Methods of Detecting Noncancerous colon Diseases

The present invention also provides methods for determining the expression levels
5 and/or structural alterations of one or more CSNAs and/or CSPs in a sample from a patient suspected of having or known to have a noncancerous colon disease. In general, the method comprises the steps of obtaining a sample from the patient, determining the expression level or structural alterations of a CSNA and/or CSP, comparing the expression level or structural alteration of the CSNA or CSP to a normal colon control, and then
10 ascertaining whether the patient has a noncancerous colon disease. In general, if high expression relative to a control of a CSNA or CSP is indicative of a particular noncancerous colon disease, a diagnostic assay is considered positive if the level of expression of the CSNA or CSP is at least two times higher, and more preferably are at least five times higher, even more preferably at least ten times higher, than in preferably
15 the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of a CSNA or CSP is indicative of a noncancerous colon disease, a diagnostic assay is considered positive if the level of expression of the CSNA or CSP is at least two times lower, more preferably are at least five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid
20 of a normal human control. The normal human control may be from a different patient or from uninvolved tissue of the same patient.

One having ordinary skill in the art may determine whether a CSNA and/or CSP is associated with a particular noncancerous colon disease by obtaining colon tissue from a patient having a noncancerous colon disease of interest and determining which CSNAs
25 and/or CSPs are expressed in the tissue at either a higher or a lower level than in normal colon tissue. In another embodiment, one may determine whether a CSNA or CSP exhibits structural alterations in a particular noncancerous colon disease state by obtaining colon tissue from a patient having a noncancerous colon disease of interest and determining the structural alterations in one or more CSNAs and/or CSPs relative to
30 normal colon tissue.

Methods for Identifying colon Tissue

In another aspect, the invention provides methods for identifying colon tissue. These methods are particularly useful in, *e.g.*, forensic science, colon cell differentiation and development, and in tissue engineering.

- 5 In one embodiment, the invention provides a method for determining whether a sample is colon tissue or has colon tissue-like characteristics. The method comprises the steps of providing a sample suspected of comprising colon tissue or having colon tissue-like characteristics, determining whether the sample expresses one or more CSNAs and/or CSPs, and, if the sample expresses one or more CSNAs and/or CSPs, concluding that the
- 10 sample comprises colon tissue. In a preferred embodiment, the CSNA encodes a polypeptide having an amino acid sequence selected from SEQ ID NO: 95-248, or a homolog, allelic variant or fragment thereof. In a more preferred embodiment, the CSNA has a nucleotide sequence selected from SEQ ID NO: 1-94, or a hybridizing nucleic acid, an allelic variant or a part thereof. Determining whether a sample expresses a CSNA can
- 15 be accomplished by any method known in the art. Preferred methods include hybridization to microarrays, Northern blot hybridization, and quantitative or qualitative RT-PCR. In another preferred embodiment, the method can be practiced by determining whether a CSP is expressed. Determining whether a sample expresses a CSP can be accomplished by any method known in the art. Preferred methods include Western blot,
- 20 ELISA, RIA and 2D PAGE. In one embodiment, the CSP has an amino acid sequence selected from SEQ ID NO: 95-248, or a homolog, allelic variant or fragment thereof. In another preferred embodiment, the expression of at least two CSNAs and/or CSPs is determined. In a more preferred embodiment, the expression of at least three, more preferably four and even more preferably five CSNAs and/or CSPs are determined.
- 25 In one embodiment, the method can be used to determine whether an unknown tissue is colon tissue. This is particularly useful in forensic science, in which small, damaged pieces of tissues that are not identifiable by microscopic or other means are recovered from a crime or accident scene. In another embodiment, the method can be used to determine whether a tissue is differentiating or developing into colon tissue. This
- 30 is important in monitoring the effects of the addition of various agents to cell or tissue culture, *e.g.*, in producing new colon tissue by tissue engineering. These agents include, *e.g.*, growth and differentiation factors, extracellular matrix proteins and culture medium. Other factors that may be measured for effects on tissue development and differentiation

include gene transfer into the cells or tissues, alterations in pH, aqueous:air interface and various other culture conditions.

Methods for Producing and Modifying colon Tissue

In another aspect, the invention provides methods for producing engineered colon
5 tissue or cells. In one embodiment, the method comprises the steps of providing cells, introducing a CSNA or a CSG into the cells, and growing the cells under conditions in which they exhibit one or more properties of colon tissue cells. In a preferred embodiment, the cells are pluripotent. As is well known in the art, normal colon tissue comprises a large number of different cell types. Thus, in one embodiment, the
10 engineered colon tissue or cells comprises one of these cell types. In another embodiment, the engineered colon tissue or cells comprises more than one colon cell type. Further, the culture conditions of the cells or tissue may require manipulation in order to achieve full differentiation and development of the colon cell tissue. Methods for manipulating culture conditions are well known in the art.

15 Nucleic acid molecules encoding one or more CSPs are introduced into cells, preferably pluripotent cells. In a preferred embodiment, the nucleic acid molecules encode CSPs having amino acid sequences selected from SEQ ID NO: 95-248, or homologous proteins, analogs, allelic variants or fragments thereof. In a more preferred embodiment, the nucleic acid molecules have a nucleotide sequence selected from SEQ ID
20 NO: 1-94, or hybridizing nucleic acids, allelic variants or parts thereof. In another highly preferred embodiment, a CSG is introduced into the cells. Expression vectors and methods of introducing nucleic acid molecules into cells are well known in the art and are described in detail, *supra*.

25 Artificial colon tissue may be used to treat patients who have lost some or all of their colon function.

Pharmaceutical Compositions

In another aspect, the invention provides pharmaceutical compositions comprising the nucleic acid molecules, polypeptides, fusion proteins, antibodies, antibody derivatives, antibody fragments, agonists, antagonists, or inhibitors of the present invention. In a
30 preferred embodiment, the pharmaceutical composition comprises a CSNA or part thereof. In a more preferred embodiment, the CSNA has a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-94, a nucleic acid that hybridizes thereto, an allelic

variant thereof, or a nucleic acid that has substantial sequence identity thereto. In another preferred embodiment, the pharmaceutical composition comprises a CSP or fragment thereof. In a more preferred embodiment, the pharmaceutical composition comprises a CSP having an amino acid sequence that is selected from the group consisting of SEQ ID NO: 95-248, a polypeptide that is homologous thereto, a fusion protein comprising all or a portion of the polypeptide, or an analog or derivative thereof. In another preferred embodiment, the pharmaceutical composition comprises an anti-CSP antibody, preferably an antibody that specifically binds to a CSP having an amino acid that is selected from the group consisting of SEQ ID NO: 95-248, or an antibody that binds to a polypeptide that is homologous thereto, a fusion protein comprising all or a portion of the polypeptide, or an analog or derivative thereof.

Due to the association of angiogenesis with cancer vascularization there is great need of new markers and methods for diagnosing angiogenesis activity to identify developing tumors and angiogenesis related diseases. Furthermore, great need is also present for new molecular targets useful in the treatment of angiogenesis and angiogenesis related diseases such as cancer. In addition known modulators of angiogenesis such as endostatin or vascular endothelial growth factor (VEGF). Use of the methods and compositions disclosed herein in combination with anti-angiogenesis drugs, drugs that block the matrix breakdown (such as BMS-275291, Dalteparin (Fragmin®), Suramin), drugs that inhibit endothelial cells (2-methoxyestradiol (2-ME), CC-5013 (Thalidomide Analog), Combretastatin A4 Phosphate, LY317615 (Protein Kinase C Beta Inhibitor), Soy Isoflavone (Genistein; Soy Protein Isolate), Thalidomide), drugs that block activators of angiogenesis (AE-941 (Neovastat™; GW786034), Anti-VEGF Antibody (Bevacizumab; Avastin™), Interferon-alpha, PTK787/ZK 222584, VEGF-Trap, ZD6474), Drugs that inhibit endothelial-specific integrin/survival signaling (EMD 121974, Anti-Anb3 Integrin Antibody (Medi-522; Vitaxin™)).

Such a composition typically contains from about 0.1 to 90% by weight of a therapeutic agent of the invention formulated in and/or with a pharmaceutically acceptable carrier or excipient.

Pharmaceutical formulation is a well-established art that is further described in Gennaro (ed.), Remington: The Science and Practice of Pharmacy, 20th ed., Lippincott, Williams & Wilkins (2000); Ansel *et al.*, Pharmaceutical Dosage Forms and Drug Delivery Systems, 7th ed., Lippincott Williams & Wilkins (1999); and Kibbe (ed.),

Handbook of Pharmaceutical Excipients American Pharmaceutical Association, 3rd ed. (2000) and thus need not be described in detail herein.

Briefly, formulation of the pharmaceutical compositions of the present invention will depend upon the route chosen for administration. The pharmaceutical compositions
5 utilized in this invention can be administered by various routes including both enteral and parenteral routes, including oral, intravenous, intramuscular, subcutaneous, inhalation, topical, sublingual, rectal, intra-arterial, intramedullary, intrathecal, intraventricular, transmucosal, transdermal, intranasal, intraperitoneal, intrapulmonary, and intrauterine.

Oral dosage forms can be formulated as tablets, pills, dragees, capsules, liquids,
10 gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Solid formulations of the compositions for oral administration can contain suitable carriers or excipients, such as carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, or sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethyl-cellulose, sodium
15 carboxymethylcellulose, or microcrystalline cellulose; gums including arabic and tragacanth; proteins such as gelatin and collagen; inorganics, such as kaolin, calcium carbonate, dicalcium phosphate, sodium chloride; and other agents such as acacia and alginic acid.

Agents that facilitate disintegration and/or solubilization can be added, such as the
20 cross-linked polyvinyl pyrrolidone, agar, alginic acid, or a salt thereof, such as sodium alginate, microcrystalline cellulose, cornstarch, sodium starch glycolate, and alginic acid.

Tablet binders that can be used include acacia, methylcellulose, sodium carboxymethylcellulose, polyvinylpyrrolidone (PovidoneTM), hydroxypropyl methylcellulose, sucrose, starch and ethylcellulose.

25 Lubricants that can be used include magnesium stearates, stearic acid, silicone fluid, talc, waxes, oils, and colloidal silica.

Fillers, agents that facilitate disintegration and/or solubilization, tablet binders and lubricants, including the aforementioned, can be used singly or in combination.

Solid oral dosage forms need not be uniform throughout. For example, dragee
30 cores can be used in conjunction with suitable coatings, such as concentrated sugar solutions, which can also contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures.

Oral dosage forms of the present invention include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with a filler or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft capsules, the active compounds can be dissolved or suspended in suitable liquids, such as fatty oils, liquid, or liquid polyethylene glycol with or without stabilizers.

Additionally, dyestuffs or pigments can be added to the tablets or dragee coatings for product identification or to characterize the quantity of active compound, *i.e.*, dosage.

Liquid formulations of the pharmaceutical compositions for oral (enteral) administration are prepared in water or other aqueous vehicles and can contain various suspending agents such as methylcellulose, alginates, tragacanth, pectin, kelgin, carrageenan, acacia, polyvinylpyrrolidone, and polyvinyl alcohol. The liquid formulations can also include solutions, emulsions, syrups and elixirs containing, together with the active compound(s), wetting agents, sweeteners, and coloring and flavoring agents.

The pharmaceutical compositions of the present invention can also be formulated for parenteral administration. Formulations for parenteral administration can be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions.

For intravenous injection, water soluble versions of the compounds of the present invention are formulated in, or if provided as a lyophilate, mixed with, a physiologically acceptable fluid vehicle, such as 5% dextrose ("D5"), physiologically buffered saline, 0.9% saline, Hanks' solution, or Ringer's solution. Intravenous formulations may include carriers, excipients or stabilizers including, without limitation, calcium, human serum albumin, citrate, acetate, calcium chloride, carbonate, and other salts.

Intramuscular preparations, *e.g.* a sterile formulation of a suitable soluble salt form of the compounds of the present invention, can be dissolved and administered in a pharmaceutical excipient such as Water-for-Injection, 0.9% saline, or 5% glucose solution. Alternatively, a suitable insoluble form of the compound can be prepared and administered as a suspension in an aqueous base or a pharmaceutically acceptable oil base, such as an ester of a long chain fatty acid (*e.g.*, ethyl oleate), fatty oils such as sesame oil, triglycerides, or liposomes.

Parenteral formulations of the compositions can contain various carriers such as vegetable oils, dimethylacetamide, dimethylformamide, ethyl lactate, ethyl carbonate,

isopropyl myristate, ethanol, polyols (glycerol, propylene glycol, liquid polyethylene glycol, and the like).

Aqueous injection suspensions can also contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran.

- 5 Non-lipid polycationic amino polymers can also be used for delivery. Optionally, the suspension can also contain suitable stabilizers or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

- Pharmaceutical compositions of the present invention can also be formulated to permit injectable, long-term, deposition. Injectable depot forms may be made by forming
10 microencapsulated matrices of the compound in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in microemulsions that
15 are compatible with body tissues.

- The pharmaceutical compositions of the present invention can be administered topically. For topical use the compounds of the present invention can also be prepared in suitable forms to be applied to the skin, or mucus membranes of the nose and throat, and can take the form of lotions, creams, ointments, liquid sprays or inhalants, drops, tinctures,
20 lozenges, or throat paints. Such topical formulations further can include chemical compounds such as dimethylsulfoxide (DMSO) to facilitate surface penetration of the active ingredient. In other transdermal formulations, typically in patch-delivered formulations, the pharmaceutically active compound is formulated with one or more skin penetrants, such as 2-N-methyl-pyrrolidone (NMP) or Azone. A topical semi-solid
25 ointment formulation typically contains a concentration of the active ingredient from about 1 to 20%, e.g., 5 to 10%, in a carrier such as a pharmaceutical cream base.

For application to the eyes or ears, the compounds of the present invention can be presented in liquid or semi-liquid form formulated in hydrophobic or hydrophilic bases as ointments, creams, lotions, paints or powders.

- 30 For rectal administration the compounds of the present invention can be administered in the form of suppositories admixed with conventional carriers such as cocoa butter, wax or other glyceride.

Inhalation formulations can also readily be formulated. For inhalation, various powder and liquid formulations can be prepared. For aerosol preparations, a sterile formulation of the compound or salt form of the compound may be used in inhalers, such as metered dose inhalers, and nebulizers. Aerosolized forms may be especially useful for treating respiratory disorders.

Alternatively, the compounds of the present invention can be in powder form for reconstitution in the appropriate pharmaceutically acceptable carrier at the time of delivery.

The pharmaceutically active compound in the pharmaceutical compositions of the present invention can be provided as the salt of a variety of acids, including but not limited to hydrochloric, sulfuric, acetic, lactic, tartaric, malic, and succinic acid. Salts tend to be more soluble in aqueous or other protonic solvents than are the corresponding free base forms.

After pharmaceutical compositions have been prepared, they are packaged in an appropriate container and labeled for treatment of an indicated condition.

The active compound will be present in an amount effective to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the art.

A "therapeutically effective dose" refers to that amount of active ingredient, for example CSP polypeptide, fusion protein, or fragments thereof, antibodies specific for CSP, agonists, antagonists or inhibitors of CSP, which ameliorates the signs or symptoms of the disease or prevent progression thereof; as would be understood in the medical arts, cure, although desired, is not required.

The therapeutically effective dose of the pharmaceutical agents of the present invention can be estimated initially by *in vitro* tests, such as cell culture assays, followed by assay in model animals, usually mice, rats, rabbits, dogs, or pigs. The animal model can also be used to determine an initial preferred concentration range and route of administration.

For example, the ED50 (the dose therapeutically effective in 50% of the population) and LD50 (the dose lethal to 50% of the population) can be determined in one or more cell culture of animal model systems. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as LD50/ED50. Pharmaceutical compositions that exhibit large therapeutic indices are preferred.

The data obtained from cell culture assays and animal studies are used in formulating an initial dosage range for human use, and preferably provide a range of circulating concentrations that includes the ED50 with little or no toxicity. After administration, or between successive administrations, the circulating concentration of active agent varies within this range depending upon pharmacokinetic factors well known in the art, such as the dosage form employed, sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors specific to the subject requiring treatment. Factors that can be taken into account by the practitioner include the severity of the disease state, general health of the subject, age, weight, gender of the subject, diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy. Long-acting pharmaceutical compositions can be administered every 3 to 4 days, every week, or once every two weeks depending on half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from 0.1 to 100,000 micrograms, up to a total dose of about 1 g, depending upon the route of administration. Where the therapeutic agent is a protein or antibody of the present invention, the therapeutic protein or antibody agent typically is administered at a daily dosage of 0.01 mg to 30 mg/kg of body weight of the patient (*e.g.*, 1mg/kg to 5 mg/kg). The pharmaceutical formulation can be administered in multiple doses per day, if desired, to achieve the total desired daily dose.

Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

Conventional methods, known to those of ordinary skill in the art of medicine, can be used to administer the pharmaceutical formulation(s) of the present invention to the patient. The pharmaceutical compositions of the present invention can be administered alone, or in combination with other therapeutic agents or interventions.

30 Therapeutic Methods

The present invention further provides methods of treating subjects having defects in a gene of the invention, *e.g.*, in expression, activity, distribution, localization, and/or

solubility, which can manifest as a disorder of colon function. As used herein, "treating" includes all medically-acceptable types of therapeutic intervention, including palliation and prophylaxis (prevention) of disease. The term "treating" encompasses any improvement of a disease, including minor improvements. These methods are discussed
5 below.

Gene Therapy and Vaccines

The isolated nucleic acids of the present invention can also be used to drive *in vivo* expression of the polypeptides of the present invention. *In vivo* expression can be driven from a vector, typically a viral vector, often a vector based upon a replication incompetent
10 retrovirus, an adenovirus, or an adeno-associated virus (AAV), for the purpose of gene therapy. *In vivo* expression can also be driven from signals endogenous to the nucleic acid or from a vector, often a plasmid vector, such as pVAX1 (Invitrogen, Carlsbad, CA, USA), for purpose of "naked" nucleic acid vaccination, as further described in U.S. Patent Nos. 5,589,466; 5,679,647; 5,804,566; 5,830,877; 5,843,913; 5,880,104; 5,958,891;
15 5,985,847; 6,017,897; 6,110,898; 6,204,250, the disclosures of which are incorporated herein by reference in their entireties. For cancer therapy, it is preferred that the vector also be tumor-selective. *See, e.g., Doronin et al., J. Virol.* 75: 3314-24 (2001).

In another embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising a nucleic
20 acid molecule of the present invention is administered. The nucleic acid molecule can be delivered in a vector that drives expression of a CSP, fusion protein, or fragment thereof, or without such vector. Nucleic acid compositions that can drive expression of a CSP are administered, for example, to complement a deficiency in the native CSP, or as DNA vaccines. Expression vectors derived from virus, replication deficient retroviruses,
25 adenovirus, adeno-associated (AAV) virus, herpes virus, or vaccinia virus can be used as can plasmids. *See, e.g., Cid-Arregui, supra.* In a preferred embodiment, the nucleic acid molecule encodes a CSP having the amino acid sequence of SEQ ID NO: 95-248, or a fragment, fusion protein, allelic variant or homolog thereof.

In still other therapeutic methods of the present invention, pharmaceutical
30 compositions comprising host cells that express a CSP, fusions, or fragments thereof can be administered. In such cases, the cells are typically autologous, so as to circumvent xenogeneic or allotypic rejection, and are administered to complement defects in CSP

production or activity. In a preferred embodiment, the nucleic acid molecules in the cells encode a CSP having the amino acid sequence of SEQ ID NO: 95-248, or a fragment, fusion protein, allelic variant or homolog thereof.

Antisense Administration

5 Antisense nucleic acid compositions, or vectors that drive expression of a CSG antisense nucleic acid, are administered to downregulate transcription and/or translation of a CSG in circumstances in which excessive production, or production of aberrant protein, is the pathophysiologic basis of disease.

Antisense compositions useful in therapy can have a sequence that is
10 complementary to coding or to noncoding regions of a CSG. For example, oligonucleotides derived from the transcription initiation site, *e.g.*, between positions -10 and +10 from the start site, are preferred.

Catalytic antisense compositions, such as ribozymes, that are capable of sequence-specific hybridization to CSG transcripts, are also useful in therapy. *See, e.g.*,
15 Phylactou, *Adv. Drug Deliv. Rev.* 44(2-3): 97-108 (2000); Phylactou *et al.*, *Hum. Mol. Genet.* 7(10): 1649-53 (1998); Rossi, *Ciba Found. Symp.* 209: 195-204 (1997); and Sigurdsson *et al.*, *Trends Biotechnol.* 13(8): 286-9 (1995).

Other nucleic acids useful in the therapeutic methods of the present invention are those that are capable of triplex helix formation in or near the CSG genomic locus. Such
20 triplexing oligonucleotides are able to inhibit transcription. *See, e.g.*, Intody *et al.*, *Nucleic Acids Res.* 28(21): 4283-90 (2000); and McGuffie *et al.*, *Cancer Res.* 60(14): 3790-9 (2000). Pharmaceutical compositions comprising such triplex forming oligos (TFOs) are administered in circumstances in which excessive production, or production of aberrant protein, is a pathophysiologic basis of disease.

25 In a preferred embodiment, the antisense molecule is derived from a nucleic acid molecule encoding a CSP, preferably a CSP comprising an amino acid sequence of SEQ ID NO: 95-248, or a fragment, allelic variant or homolog thereof. In a more preferred embodiment, the antisense molecule is derived from a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-94, or a part, allelic variant, substantially similar or
30 hybridizing nucleic acid thereof.

Polypeptide Administration

In one embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising a CSP, a fusion protein, fragment, analog or derivative thereof is administered to a subject with a clinically-significant CSP defect.

- 5 Protein compositions are administered, for example, to complement a deficiency in native CSP. In other embodiments, protein compositions are administered as a vaccine to elicit a humoral and/or cellular immune response to CSP. The immune response can be used to modulate activity of CSP or, depending on the immunogen, to immunize against aberrant or aberrantly expressed forms, such as mutant or inappropriately expressed
- 10 isoforms. In yet other embodiments, protein fusions having a toxic moiety are administered to ablate cells that aberrantly accumulate CSP.

- In a preferred embodiment, the polypeptide administered is a CSP comprising an amino acid sequence of SEQ ID NO: 95-248, or a fusion protein, allelic variant, homolog, analog or derivative thereof. In a more preferred embodiment, the polypeptide is encoded
- 15 by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-94, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

Antibody, Agonist and Antagonist Administration

- In another embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising an antibody
- 20 (including fragment or derivative thereof) of the present invention is administered. As is well known, antibody compositions are administered, for example, to antagonize activity of CSP, or to target therapeutic agents to sites of CSP presence and/or accumulation. In a preferred embodiment, the antibody specifically binds to a CSP comprising an amino acid sequence of SEQ ID NO: 95-248, or a fusion protein, allelic variant, homolog, analog or
- 25 derivative thereof. In a more preferred embodiment, the antibody specifically binds to a CSP encoded by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-94, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

- The present invention also provides methods for identifying modulators which bind to a CSP or have a modulatory effect on the expression or activity of a CSP.
- 30 Modulators which decrease the expression or activity of CSP (antagonists) are believed to be useful in treating colon cancer. Such screening assays are known to those of skill in the art and include, without limitation, cell-based assays and cell-free assays. Small molecules

predicted via computer imaging to specifically bind to regions of a CSP can also be designed, synthesized and tested for use in the imaging and treatment of colon cancer. Further, libraries of molecules can be screened for potential anticancer agents by assessing the ability of the molecule to bind to the CSPs identified herein. Molecules identified in the library as being capable of binding to a CSP are key candidates for further evaluation for use in the treatment of colon cancer. In a preferred embodiment, these molecules will downregulate expression and/or activity of a CSP in cells.

In another embodiment of the therapeutic methods of the present invention, a pharmaceutical composition comprising a non-antibody antagonist of CSP is administered. Antagonists of CSP can be produced using methods generally known in the art. In particular, purified CSP can be used to screen libraries of pharmaceutical agents, often combinatorial libraries of small molecules, to identify those that specifically bind and antagonize at least one activity of a CSP.

In other embodiments a pharmaceutical composition comprising an agonist of a CSP is administered. Agonists can be identified using methods analogous to those used to identify antagonists.

In a preferred embodiment, the antagonist or agonist specifically binds to and antagonizes or agonizes, respectively, a CSP comprising an amino acid sequence of SEQ ID NO: 95-248, or a fusion protein, allelic variant, homolog, analog or derivative thereof. In a more preferred embodiment, the antagonist or agonist specifically binds to and antagonizes or agonizes, respectively, a CSP encoded by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-94, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

Targeting Colon Tissue

The invention also provides a method in which a polypeptide of the invention, or an antibody thereto, is linked to a therapeutic agent such that it can be delivered to the colon or to specific cells in the colon. In a preferred embodiment, an anti-CSP antibody is linked to a therapeutic agent and is administered to a patient in need of such therapeutic agent. The therapeutic agent may be a toxin, if colon tissue needs to be selectively destroyed. This would be useful for targeting and killing colon cancer cells. In another embodiment, the therapeutic agent may be a growth or differentiation factor, which would be useful for promoting colon cell function.

In another embodiment, an anti-CSP antibody may be linked to an imaging agent that can be detected using, *e.g.*, magnetic resonance imaging, CT or PET. This would be useful for determining and monitoring colon function, identifying colon cancer tumors, and identifying noncancerous colon diseases.

5

EXAMPLES

Example 1a: Alternative Splice Variants

We identified gene transcripts using the Gencarta™ tools (Compugen Ltd., Tel Aviv, Israel) and a variety of public and proprietary databases. These splice variants are either sequences which differ from a previously defined sequence or new uses of known sequences. In general related variants are annotated as DEX0450_XXX.nt.1, DEX0450_XXX.nt.2, DEX0450_XXX.nt.3, etc. The variant DNA sequences encode proteins which differ from a previously defined protein sequence. In relation to the nucleotide sequence naming convention, protein variants are annotated as DEX0450_XXX.aa.1, DEX0450_XXX.aa.2, etc., wherein transcript DEX0450_XXX.nt.1 encodes protein DEX0450_XXX.aa.1. A single transcript may encode a protein from an alternate Open Reading Fram (ORF) which is designated DEX0450_XXX.orf.1. Additionally, multiple transcripts may encode for a single protein. In this case, DEX0450_XXX.nt.1 and DEX0450_XXX.nt.2 will both be associated with DEX0450_XXX.aa.1.

20 The mapping of the nucleic acid ("NT") SEQ ID NO; DEX ID; chromosomal location (if known); open reading frame (ORF) location; amino acid ("AA") SEQ ID NO; AA DEX ID; are shown in the table below.

SEQ ID NO	DEX ID	Chromo Map	ORF Loc	SEQ ID NO	DEX ID
1	DEX0450_001.nt.1	6p21.31	296-932	95	DEX0450_001.aa.1
1	DEX0450_001.nt.1	6p21.31	656-1330	96	DEX0450_001.orf.1
2	DEX0450_002.nt.1	6p22.1	957-1812	97	DEX0450_002.aa.1
2	DEX0450_002.nt.1	6p22.1	847-1809	98	DEX0450_002.orf.1
3	DEX0450_003.nt.1	19q13.2	1-154	99	DEX0450_003.aa.1
3	DEX0450_003.nt.1	19q13.2	62-424	100	DEX0450_003.orf.1
4	DEX0450_003.nt.2	19q13.2	485-1642	101	DEX0450_003.aa.2
5	DEX0450_003.nt.3	19q13.2	100-674	102	DEX0450_003.aa.3
5	DEX0450_003.nt.3	19q13.2	296-1621	103	DEX0450_003.orf.3
6	DEX0450_004.nt.1	5q32	75-371	104	DEX0450_004.aa.1
7	DEX0450_005.nt.1	8q21.11	1-321	105	DEX0450_005.aa.1

7	DEX0450_005.nt.1	8q21.11	1-279	106	DEX0450_005.orf.1
8	DEX0450_006.nt.1	7q31.33	27-326	107	DEX0450_006.aa.1
9	DEX0450_007.nt.1	7	203-1876	108	DEX0450_007.orf.1
9	DEX0450_007.nt.1	7	1-1503	109	DEX0450_007.aa.1
10	DEX0450_007.nt.2	7q32.1	203-1216	110	DEX0450_007.orf.2
10	DEX0450_007.nt.2	7q32.1	1-843	111	DEX0450_007.aa.2
11	DEX0450_008.nt.1	18q21.33	239-1541	112	DEX0450_008.aa.1
12	DEX0450_009.nt.1	2q14.1	2984-5102	113	DEX0450_009.aa.1
12	DEX0450_009.nt.1	2q14.1	714-1391	114	DEX0450_009.orf.1
13	DEX0450_009.nt.2	2q14.1	550-2259	115	DEX0450_009.aa.2
14	DEX0450_010.nt.1	20p13	312-716	116	DEX0450_010.aa.1
15	DEX0450_010.nt.2	20p13	28-276	117	DEX0450_010.aa.2
15	DEX0450_010.nt.2	20p13	1-438	118	DEX0450_010.orf.2
16	DEX0450_010.nt.3	20p13	1389-3234	119	DEX0450_010.aa.3
16	DEX0450_010.nt.3	20p13	1992-3230	120	DEX0450_010.orf.3
17	DEX0450_011.nt.1	14q24.2	108-1100	121	DEX0450_011.aa.1
18	DEX0450_012.nt.1	17q12	116-643	122	DEX0450_012.aa.1
19	DEX0450_012.nt.2	17q12	116-589	123	DEX0450_012.aa.2
20	DEX0450_013.nt.1	16p13.3	358-1095	124	DEX0450_013.aa.1
21	DEX0450_014.nt.1	6p21.1	133-955	125	DEX0450_014.aa.1
21	DEX0450_014.nt.1	6p21.1	119-952	126	DEX0450_014.orf.1
22	DEX0450_015.nt.1	2p23.3	25-6947	127	DEX0450_015.aa.1
22	DEX0450_015.nt.1	2p23.3	3-4955	128	DEX0450_015.orf.1
23	DEX0450_015.nt.2	2p23.3	27-6752	129	DEX0450_015.aa.2
24	DEX0450_015.nt.3	2p23.3	642-1754	130	DEX0450_015.aa.3
25	DEX0450_016.nt.1	7q11.23	55-2968	131	DEX0450_016.aa.1
25	DEX0450_016.nt.1	7q11.23	2-2158	132	DEX0450_016.orf.1
26	DEX0450_016.nt.2	7q11.23	204-2094	133	DEX0450_016.aa.2
26	DEX0450_016.nt.2	7q11.23	139-1284	134	DEX0450_016.orf.2
27	DEX0450_016.nt.3	7q11.23	55-3085	135	DEX0450_016.aa.3
27	DEX0450_016.nt.3	7q11.23	869-2275	136	DEX0450_016.orf.3
28	DEX0450_017.nt.1	19p13.2	1-573	137	DEX0450_017.aa.1
29	DEX0450_017.nt.2	19p13.2	1-356	138	DEX0450_017.aa.2
29	DEX0450_017.nt.2	19p13.2	328-822	139	DEX0450_017.orf.2
30	DEX0450_017.nt.3	19p13.2	1-443	140	DEX0450_017.aa.3
30	DEX0450_017.nt.3	19p13.2	415-909	141	DEX0450_017.orf.3
31	DEX0450_018.nt.1	7q22.1	608-2515	142	DEX0450_018.aa.1
32	DEX0450_018.nt.2	7q22.1	608-2653	143	DEX0450_018.aa.2
33	DEX0450_018.nt.3	7q22.1	607-2570	144	DEX0450_018.aa.3
33	DEX0450_018.nt.3	7q22.1	563-2569	145	DEX0450_018.orf.3
34	DEX0450_018.nt.4	7q22.1	143-1379	146	DEX0450_018.aa.4
34	DEX0450_018.nt.4	7q22.1	612-1376	147	DEX0450_018.orf.4
35	DEX0450_019.nt.1	6p21.32	1091-2030	148	DEX0450_019.aa.1
35	DEX0450_019.nt.1	6p21.32	858-1754	149	DEX0450_019.orf.1
36	DEX0450_019.nt.2	6p21.32	1091-1912	150	DEX0450_019.aa.2
36	DEX0450_019.nt.2	6p21.32	858-1739	151	DEX0450_019.orf.2
37	DEX0450_019.nt.3	6p21.32	1091-1797	152	DEX0450_019.aa.3

37	DEX0450_019.nt.3	6p21.32	858-1748	153	DEX0450_019.orf.3
38	DEX0450_020.nt.1	10q24.32	270-1053	154	DEX0450_020.aa.1
38	DEX0450_020.nt.1	10q24.32	303-1049	155	DEX0450_020.orf.1
39	DEX0450_020.nt.2	10q24.32	823-1222	156	DEX0450_020.aa.2
39	DEX0450_020.nt.2	10q24.32	457-1131	157	DEX0450_020.orf.2
40	DEX0450_020.nt.3	10q24.32	823-1222		DEX0450_020.aa.2
40	DEX0450_020.nt.3	10q24.32	3052-4404	158	DEX0450_020.orf.3
41	DEX0450_021.nt.1	13q21.31	227-3805	159	DEX0450_021.aa.1
42	DEX0450_022.nt.1	19q13.43	359-2312	160	DEX0450_022.aa.1
42	DEX0450_022.nt.1	19q13.43	327-1433	161	DEX0450_022.orf.1
43	DEX0450_023.nt.1	6p24.3	1-492	162	DEX0450_023.aa.1
44	DEX0450_023.nt.2	6p24.3	1-96	163	DEX0450_023.aa.2
44	DEX0450_023.nt.2	6p24.3	883-1212	164	DEX0450_023.orf.2
45	DEX0450_023.nt.3	6p24.3	1-122	165	DEX0450_023.aa.3
45	DEX0450_023.nt.3	6p24.3	242-571	166	DEX0450_023.orf.3
46	DEX0450_024.nt.1	16q22.1	142-561	167	DEX0450_024.aa.1
47	DEX0450_025.nt.1	1q21.3	1-222	168	DEX0450_025.aa.1
47	DEX0450_025.nt.1	1q21.3	2-217	169	DEX0450_025.orf.1
48	DEX0450_026.nt.1	12p13.33	1-966	170	DEX0450_026.aa.1
48	DEX0450_026.nt.1	12p13.33	3-962	171	DEX0450_026.orf.1
49	DEX0450_026.nt.2	12p13.33	1-966		DEX0450_026.aa.1
49	DEX0450_026.nt.2	12p13.33	3-962	172	DEX0450_026.orf.2
50	DEX0450_027.nt.1	1p13.3	541-2592	173	DEX0450_027.aa.1
51	DEX0450_027.nt.2	1p13.3	540-2595		DEX0450_027.aa.1
52	DEX0450_028.nt.1	2q35	152-1650	174	DEX0450_028.aa.1
52	DEX0450_028.nt.1	2q35	105-1325	175	DEX0450_028.orf.1
53	DEX0450_029.nt.1	1p13.3	46-141	176	DEX0450_029.aa.1
53	DEX0450_029.nt.1	1p13.3	960-1166	177	DEX0450_029.orf.1
54	DEX0450_030.nt.1	1q32.2	1-265	178	DEX0450_030.aa.1
54	DEX0450_030.nt.1	1q32.2	7-264	179	DEX0450_030.orf.1
55	DEX0450_031.nt.1	5q32	98-1313	180	DEX0450_031.aa.1
55	DEX0450_031.nt.1	5q32	196-1308	181	DEX0450_031.orf.1
56	DEX0450_031.nt.2	5q32	1-309	182	DEX0450_031.aa.2
56	DEX0450_031.nt.2	5q32	308-613	183	DEX0450_031.orf.2
57	DEX0450_032.nt.1	19p13.3	58-881	184	DEX0450_032.aa.1
57	DEX0450_032.nt.1	19p13.3	197-877	185	DEX0450_032.orf.1
58	DEX0450_032.nt.2	19p13.3	37-1396	186	DEX0450_032.aa.2
58	DEX0450_032.nt.2	19p13.3	481-1392	187	DEX0450_032.orf.2
59	DEX0450_032.nt.3	19p13.3	37-1858	188	DEX0450_032.aa.3
59	DEX0450_032.nt.3	19p13.3	481-1161	189	DEX0450_032.orf.3
60	DEX0450_032.nt.4	19p13.3	37-1336	190	DEX0450_032.aa.4
60	DEX0450_032.nt.4	19p13.3	481-1332	191	DEX0450_032.orf.4
61	DEX0450_032.nt.5	19p13.3	37-1396		DEX0450_032.aa.2
61	DEX0450_032.nt.5	19p13.3	481-1392	192	DEX0450_032.orf.5
62	DEX0450_032.nt.6	19p13.3	37-1396		DEX0450_032.aa.2
62	DEX0450_032.nt.6	19p13.3	481-1392	193	DEX0450_032.orf.6
63	DEX0450_032.nt.7	19p13.3	37-1396		DEX0450_032.aa.2

63	DEX0450_032.nt.7	19p13.3	481-1392	194	DEX0450_032.orf.7
64	DEX0450_033.nt.1	12q13.13	3-944	195	DEX0450_033.aa.1
64	DEX0450_033.nt.1	12q13.13	3-890	196	DEX0450_033.orf.1
65	DEX0450_033.nt.2	12q13.13	73-877	197	DEX0450_033.aa.2
65	DEX0450_033.nt.2	12q13.13	2-1363	198	DEX0450_033.orf.2
66	DEX0450_034.nt.1	12q13.13	362-673	199	DEX0450_034.aa.1
67	DEX0450_035.nt.1	1q44	76-2383	200	DEX0450_035.aa.1
67	DEX0450_035.nt.1	1q44	1-2379	201	DEX0450_035.orf.1
68	DEX0450_036.nt.1	13q13.3	413-1387	202	DEX0450_036.aa.1
69	DEX0450_037.nt.1	4q22.1	88-483	203	DEX0450_037.aa.1
69	DEX0450_037.nt.1	4q22.1	132-479	204	DEX0450_037.orf.1
70	DEX0450_038.nt.1	X;116878557-116901416	560-752	205	DEX0450_038.aa.1
70	DEX0450_038.nt.1	X;116878557-116901416	562-852	206	DEX0450_038.orf.1
71	DEX0450_039.nt.1	9p13.3	367-853	207	DEX0450_039.aa.1
71	DEX0450_039.nt.1	9p13.3	3-851	208	DEX0450_039.orf.1
72	DEX0450_039.nt.2	9p13.3	163-833	209	DEX0450_039.aa.2
72	DEX0450_039.nt.2	9p13.3	37-786	210	DEX0450_039.orf.2
73	DEX0450_039.nt.3	9p13.3	1-431	211	DEX0450_039.aa.3
73	DEX0450_039.nt.3	9p13.3	3-662	212	DEX0450_039.orf.3
74	DEX0450_039.nt.4	9p13.3	602-938	213	DEX0450_039.aa.4
74	DEX0450_039.nt.4	9p13.3	226-933	214	DEX0450_039.orf.4
75	DEX0450_039.nt.5	9p13.3	602-1233	215	DEX0450_039.aa.5
75	DEX0450_039.nt.5	9p13.3	226-1014	216	DEX0450_039.orf.5
76	DEX0450_039.nt.6	9p13.3	602-1055	217	DEX0450_039.aa.6
76	DEX0450_039.nt.6	9p13.3	226-1032	218	DEX0450_039.orf.6
77	DEX0450_040.nt.1	12q15	43-498	219	DEX0450_040.aa.1
78	DEX0450_041.nt.1	19q13.41	1-538	220	DEX0450_041.aa.1
78	DEX0450_041.nt.1	19q13.41	234-782	221	DEX0450_041.orf.1
79	DEX0450_042.nt.1	10q24.32	55-2283	222	DEX0450_042.aa.1
80	DEX0450_042.nt.2	10q24.32	1-867	223	DEX0450_042.aa.2
80	DEX0450_042.nt.2	10q24.32	69-863	224	DEX0450_042.orf.2
81	DEX0450_043.nt.1	2p15	2430-6261	225	DEX0450_043.aa.1
81	DEX0450_043.nt.1	2p15	4360-6255	226	DEX0450_043.orf.1
82	DEX0450_044.nt.1	X;150551654-150555252	82-562	227	DEX0450_044.aa.1
83	DEX0450_044.nt.2	X;150551654-150575564	1038-1976	228	DEX0450_044.aa.2
84	DEX0450_044.nt.3	X;150551654-150575855	409-1311	229	DEX0450_044.aa.3
85	DEX0450_045.nt.1	12q13.2	1-299	230	DEX0450_045.aa.1
85	DEX0450_045.nt.1	12q13.2	4-393	231	DEX0450_045.orf.1
86	DEX0450_046.nt.1	17q25.3	3-786	232	DEX0450_046.aa.1
86	DEX0450_046.nt.1	17q25.3	35-763	233	DEX0450_046.orf.1
87	DEX0450_047.nt.1	19p13.3	88-1375	234	DEX0450_047.aa.1
87	DEX0450_047.nt.1	19p13.3	487-1347	235	DEX0450_047.orf.1
88	DEX0450_048.nt.1	2p13.2	22-766	236	DEX0450_048.aa.1

88	DEX0450_048.nt.1	2p13.2	290-751	237	DEX0450_048.orf.1
89	DEX0450_049.nt.1	7q22.1	139-944	238	DEX0450_049.aa.1
89	DEX0450_049.nt.1	7q22.1	505-918	239	DEX0450_049.orf.1
90	DEX0450_050.nt.1	8q22.1	268-970	240	DEX0450_050.aa.1
90	DEX0450_050.nt.1	8q22.1	15-971	241	DEX0450_050.orf.1
91	DEX0450_051.nt.1	8p23.1	58-287	242	DEX0450_051.aa.1
91	DEX0450_051.nt.1	8p23.1	2-217	243	DEX0450_051.orf.1
92	DEX0450_051.nt.2	8p23.1	49-235	244	DEX0450_051.aa.2
92	DEX0450_051.nt.2	8p23.1	63-233	245	DEX0450_051.orf.2
93	DEX0450_052.nt.1	9q34.11	1-797	246	DEX0450_052.aa.1
93	DEX0450_052.nt.1	9q34.11	322-765	247	DEX0450_052.orf.1
94	DEX0450_053.nt.1	8q22.1	244-945	248	DEX0450_053.aa.1

The polypeptides of the present invention were analyzed and the following attributes were identified; specifically, epitopes, post translational modifications, signal peptides and transmembrane domains. Antigenicity (Epitope) prediction was performed through the antigenic module in the EMBOSS package. Rice, P., EMBOSS: The European Molecular Biology Open Software Suite, *Trends in Genetics* 16(6): 276-277 (2000). The antigenic module predicts potentially antigenic regions of a protein sequence, using the method of Kolaskar and Tongaonkar. Kolaskar, AS and Tongaonkar, PC., A semi-empirical method for prediction of antigenic determinants on protein antigens, *FEBS Letters* 276: 172-174 (1990). Examples of post-translational modifications (PTMs) and other motifs of the CSPs of this invention are listed below. In addition, antibodies that specifically bind such post-translational modifications may be useful as a diagnostic or as therapeutic. The PTMs and other motifs were predicted by using the ProSite Dictionary of Proteins Sites and Patterns (Bairoch *et al.*, *Nucleic Acids Res.* 25(1):217-221 (1997)), the following motifs, including PTMs, were predicted for the CSPs of the invention. The signal peptides were detected by using the SignalP 2.0, *see* Nielsen *et al.*, *Protein Engineering* 12, 3-9 (1999). Prediction of transmembrane helices in proteins was performed by the application TMHMM 2.0, "currently the best performing transmembrane prediction program", according to authors (Krogh *et al.*, *Journal of Molecular Biology*, 305(3):567-580, (2001); Moller *et al.*, *Bioinformatics*, 17(7):646-653, (2001); Sonnhammer, *et al.*, *A hidden Markov model for predicting transmembrane helices in protein sequences* in Glasgow, *et al.* Ed. Proceedings of the Sixth International Conference on Intelligent Systems for Molecular Biology, pages 175-182, Menlo Park, CA, 1998. AAAI Press. The PSORT II program may also be used to predict cellular localizations. Horton *et al.*, *Intelligent Systems for Molecular Biology* 5: 147-152 (1997).

The table below includes the following sequence annotations: Signal peptide presence; TM (number of membrane domain, topology in orientation and position); Amino acid location and antigenic index (location, AI score); PTM and other motifs (type, amino acid residue locations); and functional domains (type, amino acid residue locations).

DEX ID	Sig P	TMHMM	Antigenicity	PTM	Domains
DEX0450-001.aa.1	N	0 - ol-211;	15-22,1.083; 60-68,1.134; 75-82,1.087; 35-44,1.142; 96-102,1.087; 126-170,1.185; 24-29,1.034; 177-208,1.233; 109-118,1.058; 50-56,1.081;	CK2_PHOSPHO_SITE 117-120; MYRISTYL 122-127; PKC_PHOSPHO_SITE 194-196; MYRISTYL 175-180; CK2_PHOSPHO_SITE 21-24;	BCL2_FAMILY 78-179; BCL 78-177; BCL-2 78-177; BH3 74-88; BH1 118-136;
DEX0450-001.orf.1	N	0 - ol-225;	145-181,1.146; 119-134,1.143; 4-11,1.088; 196-222,1.177; 38-55,1.213; 66-100,1.17; 13-28,1.055;	CK2_PHOSPHO_SITE 109-112; MYRISTYL 186-191; MYRISTYL 116-121; MYRISTYL 9-14; MYRISTYL 144-149; LEUCINE_ZIPPER 16-37; MYRISTYL 71-76; PKC_PHOSPHO_SITE 135-137; MYRISTYL 185-190; MYRISTYL 189-194; MYRISTYL 115-120;	
DEX0450-002.aa.1	N	0 - ol-284;	40-64,1.145; 155-167,1.188; 255-264,1.165; 188-213,1.111; 81-92,1.153; 177-183,1.094; 127-141,1.201; 18-29,1.144; 215-250,1.119; 96-117,1.136; 143-149,1.09;	PKC_PHOSPHO_SITE 16-18; CAMP_PHOSPHO_SITE 11-14; ASN_GLYCOSYLATION 222-225; MYRISTYL 167-172; MYRISTYL 9-14; PKC_PHOSPHO_SITE 66-68; CK2_PHOSPHO_SITE 71-74; PKC_PHOSPHO_SITE 61-63; PKC_PHOSPHO_SITE 224-226; CK2_PHOSPHO_SITE 264-267; CK2_PHOSPHO_SITE 40-43; MYRISTYL 251-256;	BUTYPHLNCDF 124-148; B302 89-245; SPRY 139-264; PRY 86-138; SPRY 139-264; BUTYPHLNCDF 102-119; SPRY 139-264; BUTYPHLNCDF 85-102; BUTYPHLNCDF 154-167; BUTYPHLNCDF 198-222; BUTYPHLNCDF 229-247;
DEX0450-002.orf.1	N	0 - ol-321;	10-17,1.093; 292-301,1.165; 133-154,1.136; 55-66,1.144; 164-178,1.201; 180-186,1.09; 252-287,1.119; 77-101,1.145; 214-220,1.094; 192-204,1.188; 118-129,1.153; 38-44,1.108; 225-250,1.111;	CAMP_PHOSPHO_SITE 48-51; MYRISTYL 46-51; CK2_PHOSPHO_SITE 108-111; PKC_PHOSPHO_SITE 103-105; CK2_PHOSPHO_SITE 77-80; CK2_PHOSPHO_SITE 301-304; PKC_PHOSPHO_SITE 261-263; PKC_PHOSPHO_SITE 98-100; ASN_GLYCOSYLATION 259-262; MYRISTYL 204-209; MYRISTYL 288-293; PKC_PHOSPHO_SITE 53-55;	BUTYPHLNCDF 235-259; BUTYPHLNCDF 191-204; SPRY 176-301; SPRY 176-301; BUTYPHLNCDF 122-139; PRY 123-175; SPRY 176-301; B302 126-282; BUTYPHLNCDF 266-284; BUTYPHLNCDF 161-185; BUTYPHLNCDF 139-156;

134

DEX0450- 003.aa.1	N	0 - ol- 50;	4-18,1.11; 25-37,1.098;	CK2_PHOSPHO_SITE 33-36; MYRISTYL 31-36;	
DEX0450- 003.orf.1	N	0 - il- 121;	98-109,1.178; 48-66,1.112; 13-21,1.088; 71-76,1.06; 34-40,1.121;	PKC_PHOSPHO_SITE 93-95; MYRISTYL 41-46; PKC_PHOSPHO_SITE 57-59; PKC_PHOSPHO_SITE 1-3; MYRISTYL 109-114; MYRISTYL 88-93;	
DEX0450- 003.aa.2	N	0 - ol- 386;	331-341,1.115; 184-194,1.16; 196-203,1.072; 95-101,1.075; 79-85,1.049; 160-173,1.091; 14-30,1.129; 103-136,1.177; 367-378,1.132; 308-317,1.104; 145-156,1.141; 230-237,1.162; 206-222,1.204; 245-254,1.139;	CK2_PHOSPHO_SITE 39-42; MYRISTYL 56-61; MYRISTYL 218-223; PKC_PHOSPHO_SITE 271-273; ASN_GLYCOSYLATION 348-351; CK2_PHOSPHO_SITE 323-326; PKC_PHOSPHO_SITE 205-207; CK2_PHOSPHO_SITE 224-227; PKC_PHOSPHO_SITE 173-175; PKC_PHOSPHO_SITE 241-243; PKC_PHOSPHO_SITE 159-161; CK2_PHOSPHO_SITE 353-356; CK2_PHOSPHO_SITE 352-355; PKC_PHOSPHO_SITE 369-371; MYRISTYL 52-57; CK2_PHOSPHO_SITE 301-304; PKC_PHOSPHO_SITE 377-379; PKC_PHOSPHO_SITE 8-10; CK2_PHOSPHO_SITE 285-288; CK2_PHOSPHO_SITE 241-244; ASN_GLYCOSYLATION 279-282; PKC_PHOSPHO_SITE 85-87; MYRISTYL 44-49; MYRISTYL 360-365; CK2_PHOSPHO_SITE 171-174; CK2_PHOSPHO_SITE 205-208; PKC_PHOSPHO_SITE 18-20; CK2_PHOSPHO_SITE 47-50; MYRISTYL 270-275; CK2_PHOSPHO_SITE 225-228; PKC_PHOSPHO_SITE 72-74; PKC_PHOSPHO_SITE 49-51;	GRAM 91-158; GRAM 91-158;
DEX0450- 003.aa.3	Y	0 - ol- 190;	64-69,1.081; 124-145,1.097; 101-121,1.119; 73-86,1.112;	AMIDATION 48-51; MYRISTYL 90-95; MYRISTYL 62-67; MYRISTYL 93-98;	

135

JG17 Rec'd PCT/PTO 10 15 38 0 2003

			174-187,1.132; 5-46,1.185; 151-164,1.142;	MYRISTYL 84-89; MYRISTYL 138-143; MYRISTYL 74-79; MYRISTYL 148-153;	
DEX0450- 003.orf. 3	N	0 - ol- 442;	77-93,1.129; 421-439,1.215; 142-148,1.049; 247- 257,1.16; 371-380,1.104; 27-56,1.19; 394-404,1.115; 293-300,1.162; 208- 219,1.141; 308-317,1.139; 158-164,1.075; 7-15,1.105; 269-285,1.204; 166- 199,1.177; 223-236,1.091; 259-266,1.072;	CK2_PHOSPHO_SITE 304-307; CK2_PHOSPHO_SITE 386-389; PKC_PHOSPHO_SITE 304-306; MYRISTYL 115-120; PKC_PHOSPHO_SITE 135-137; PKC_PHOSPHO_SITE 222-224; CK2_PHOSPHO_SITE 415-418; MYRISTYL 333-338; CK2_PHOSPHO_SITE 287-290; MYRISTYL 281-286; MYRISTYL 107-112; PKC_PHOSPHO_SITE 236-238; MYRISTYL 422-427; CK2_PHOSPHO_SITE 288-291; MYRISTYL 16-21; MYRISTYL 32-37; PKC_PHOSPHO_SITE 112-114; PKC_PHOSPHO_SITE 71-73; MYRISTYL 18- 23; PKC_PHOSPHO_SITE 148-150; ASN GLYCOSYLATION 342-345; CK2_PHOSPHO_SITE 348-351; CK2_PHOSPHO_SITE 234-237; MYRISTYL 20-25; PKC_PHOSPHO_SITE 268-270; CK2_PHOSPHO_SITE 416-419; CK2_PHOSPHO_SITE 268-271; CK2_PHOSPHO_SITE 63-66; CK2_PHOSPHO_SITE 102-105; MYRISTYL 119-124; PKC_PHOSPHO_SITE 81-83; CK2_PHOSPHO_SITE 364-367; PKC_PHOSPHO_SITE 334-336; CK2_PHOSPHO_SITE 110-113; ASN GLYCOSYLATION 411-414;	GRAM 154-221; GRAM 154- 221;
DEX0450- 004.aa.1	Y	0 - ol- 99;	23-38,1.163; 49-56,1.063; 5-13,1.148; 58-69,1.138; 89-96,1.075; 76-83,1.179;	CAMP_PHOSPHO_SITE 86-89; CK2_PHOSPHO_SITE 41-44; PKC_PHOSPHO_SITE 14-16; AMIDATION 14-17; CAMP_PHOSPHO_SITE 16-19; MYRISTYL 39-44; PKC_PHOSPHO_SITE 5- 7; MYRISTYL 68-73;	KAZALINHBTR 70-81; KAZALINHBTR 59-69; KAZAL 51-99; KAZAL 59- 81; kazal 52-99;
DEX0450	N	0 - ol-	35-56.1.126; 12-29.1.12;	CK2 PHOSPHO SITE 30-33; MYRISTYL 60-	

005.aa.1	106;	80-90,1.106; 64-72,1.12;	65; CK2_PHOSPHO_SITE 91-94; PKC_PHOSPHO_SITE 21-23;	
DEX0450- 005.orf. 1	N		MICROBODIES_CTER 91-93; PKC_PHOSPHO_SITE 21-23; CK2_PHOSPHO_SITE 30-33; PKC_PHOSPHO_SITE 91-93; MYRISTYL 60-65;	
DEX0450- 006.aa.1	Y	92-97,1.054; 7-25,1.14; 27-40,1.171; 48-55,1.118; 74-81,1.098;	PKC_PHOSPHO_SITE 47-49; PKC_PHOSPHO_SITE 87-89; CAMP_PHOSPHO_SITE 44-47; ASN_GLYCOSYLATION 84-87; ASN_GLYCOSYLATION 97-100;	G_PROTEIN_RECEP_F3_4 1-49;
DEX0450- 007.orf. 1	N	91-114,1.127; 18-44,1.263; 548-555,1.106; 478-491,1.112; 357-364,1.054; 169-183,1.137; 186-191,1.104; 516-543,1.208; 130-141,1.094; 345-351,1.048; 458-475,1.157; 332-338,1.065; 65-82,1.224; 289-294,1.066; 499-506,1.108; 118-124,1.109; 299-309,1.15; 438-444,1.065; 249-270,1.144; 372-379,1.122; 383-392,1.107; 204-239,1.119; 272-278,1.113; 147-163,1.121; 49-63,1.121;	CAMP_PHOSPHO_SITE 29-32; PKC_PHOSPHO_SITE 307-309; CAMP_PHOSPHO_SITE 439-442; AMIDATION 61-64; PKC_PHOSPHO_SITE 28-30; MYRISTYL 118-123; PKC_PHOSPHO_SITE 6-8; MYRISTYL 47-52; CK2_PHOSPHO_SITE 442-445; CK2_PHOSPHO_SITE 287-290; MYRISTYL 425-430; CAMP_PHOSPHO_SITE 433-436; MYRISTYL 301-306; ASN_GLYCOSYLATION 355-358; AMIDATION 431-434; MYRISTYL 206-211; CAMP_PHOSPHO_SITE 391-394; CK2_PHOSPHO_SITE 236-239; ASN_GLYCOSYLATION 152-155; CK2_PHOSPHO_SITE 492-495; PKC_PHOSPHO_SITE 75-77; PKC_PHOSPHO_SITE 9-11; MYRISTYL 209-214; PKC_PHOSPHO_SITE 32-34; PKC_PHOSPHO_SITE 556-558; MYRISTYL 510-515; CK2_PHOSPHO_SITE 199-202; PKC_PHOSPHO_SITE 96-98; CK2_PHOSPHO_SITE 451-454; MYRISTYL 514-519; CK2_PHOSPHO_SITE 244-247; TYR_PHOSPHO_SITE 446-453;	GPCRMR 144-163; ANF_receptor 126-551; GPCRMR 100-112; ANF_receptor 126-551; GPCRMR 275-292; ANF_receptor 126-551; GPCRMR 129-144; G_PROTEIN_RECEP_F3_1 219-237; G_PROTEIN_RECEP_F3_1 219-237; MTABOTROPICR 302-313; MTABOTROPICR 319-331; G_PROTEIN_RECEP_F3_1 219-237; G_PROTEIN_RECEP_F3_1 219-237; MTABOTROPICR 454-465; ANF_receptor 126-551; ANF_receptor 126-551; ANF_receptor 126-551; GPCRMR 259-275; MTABOTROPICR 384-399; G PROTEIN RECEP F3 1

137

DEX0450- 007.aa.1	Y	0 - 01- 501;	112-126, 1.137; 61-67, 1.109; 381-387, 1.065; 442- 449, 1.108; 34-57, 1.127; 8- 25, 1.224; 459-486, 1.208; 90-106, 1.121; 300- 307, 1.054; 421-434, 1.112; 275-281, 1.065; 147- 182, 1.119; 192-213, 1.144; 288-294, 1.048; 215- 221, 1.113; 491-498, 1.106; 326-335, 1.107; 129- 134, 1.104; 315-322, 1.122; 242-252, 1.15; 73-84, 1.094; 232-237, 1.066; 401- 418, 1.157;	CK2_PHOSPHO_SITE 394-397; PKC_PHOSPHO_SITE 499-501; PKC_PHOSPHO_SITE 250-252; AMIDATION 4-7; MYRISTYL 244-249; CAMP_PHOSPHO_SITE 334-337; CK2_PHOSPHO_SITE 142-145; TYR_PHOSPHO_SITE 389-396; CK2_PHOSPHO_SITE 187-190; CK2_PHOSPHO_SITE 385-388; MYRISTYL 457-462; ASN_GLYCOSYLATION 95-98; CK2_PHOSPHO_SITE 435-438; AMIDATION 374-377; CK2_PHOSPHO_SITE 230-233; MYRISTYL 149-154; PKC_PHOSPHO_SITE 18-20; CAMP_PHOSPHO_SITE 382-385; MYRISTYL 61-66; CK2_PHOSPHO_SITE 179-182; MYRISTYL 453-458; CAMP_PHOSPHO_SITE 376-379; PKC_PHOSPHO_SITE 39-41; MYRISTYL 152-157; ASN_GLYCOSYLATION 298-301; MYRISTYL 368-373;	219-237; GPCRMR 240- 259; GPCRMR 207-233; G_PROTEIN_RECEP_F3_1 219-237; MTABOTROPICR 327-342; MTABOTROPICR 245-256; MTABOTROPICR 262-274; MTABOTROPICR 397-408; GPCRMR 43-55; GPCRMR 218-235; GPCRMR 150- 176; GPCRMR 183-202; GPCRMR 87-106; GPCRMR 202-218; GPCRMR 72-87; ANF_receptor 69-494; G_PROTEIN_RECEP_F3_1 162-180;
DEX0450- 007.orf. 2	N	0 - 01- 338;	169-183, 1.137; 118- 124, 1.109; 186-191, 1.104; 130-141, 1.094; 301- 335, 1.251; 272-278, 1.113; 18-44, 1.263; 49-63, 1.121; 249-270, 1.144; 65-82, 1.224; 147-163, 1.121; 204- 239, 1.119; 289-294, 1.066; 91-114, 1.127;	PKC_PHOSPHO_SITE 28-30; MYRISTYL 206-211; PKC_PHOSPHO_SITE 32-34; MYRISTYL 118-123; PKC_PHOSPHO_SITE 96-98; CAMP_PHOSPHO_SITE 29-32; CK2_PHOSPHO_SITE 244-247; PKC_PHOSPHO_SITE 6-8; PKC_PHOSPHO_SITE 9-11; MYRISTYL 209- 214; CK2_PHOSPHO_SITE 236-239; CK2_PHOSPHO_SITE 199-202; ASN_GLYCOSYLATION 152-155; CK2_PHOSPHO_SITE 287-290; MYRISTYL 306-311; MYRISTYL 47-52;	G_PROTEIN_RECEP_F3_1 219-237; GPCRMR 240- 259; G_PROTEIN_RECEP_F3_1 219-237; G_PROTEIN_RECEP_F3_1 219-237; G_PROTEIN_RECEP_F3_1 219-237; GPCRMR 275- 292; GPCRMR 207-233; GPCRMR 259-275; GPCRMR 129-144;

				PKC_PHOSPHO_SITE 75-77; AMIDATION 61-64;	GPCRMGR 100-112; G_PROTEIN_RECEP_F3_1 219-237; G_PROTEIN_RECEP_F3_1 219-237; GPCRMGR 144- 163;
DEX0450- 007.aa.2	Y	0 - ol- 281;	90-106,1.121; 73-84,1.094; 112-126,1.137; 34-57,1.127; 129-134,1.104; 192- 213,1.144; 232-237,1.066; 8-25,1.224; 147-182,1.119; 215-221,1.113; 244- 278,1.251; 61-67,1.109;	ASN_GLYCOSYLATION 95-98; MYRISTYL 61-66; MYRISTYL 249-254; CK2_PHOSPHO_SITE 142-145; CK2_PHOSPHO_SITE 179-182; AMIDATION 4-7; CK2_PHOSPHO_SITE 187-190; PKC_PHOSPHO_SITE 39-41; MYRISTYL 149-154; PKC_PHOSPHO_SITE 18-20; MYRISTYL 152-157; CK2_PHOSPHO_SITE 230-233;	G_PROTEIN_RECEP_F3_1 162-180; GPCRMGR 87- 106; GPCRMGR 43-55; GPCRMGR 72-87; GPCRMGR 218-235; GPCRMGR 202- 218; GPCRMGR 150-176; GPCRMGR 183-202;
DEX0450- 008.aa.1	N	0 - ol- 433;	12-29,1.113; 239-245,1.086; 342-355,1.105; 391- 403,1.094; 81-98,1.189; 216-227,1.154; 424- 430,1.092; 269-278,1.116; 42-54,1.192; 409-417,1.125; 171-177,1.04; 111- 162,1.158; 285-293,1.128; 101-108,1.081; 369- 384,1.231; 326-335,1.103; 61-67,1.046;	PKC_PHOSPHO_SITE 165-167; PKC_PHOSPHO_SITE 143-145; PKC_PHOSPHO_SITE 30-32; ASN_GLYCOSYLATION 419-422; MYRISTYL 364-369; CK2_PHOSPHO_SITE 193-196; PKC_PHOSPHO_SITE 100-102; ASN_GLYCOSYLATION 191-194; MYRISTYL 370-375; MYRISTYL 188-193; CK2_PHOSPHO_SITE 299-302; CK2_PHOSPHO_SITE 210-213; ASN_GLYCOSYLATION 246-249; PKC_PHOSPHO_SITE 166-168; MYRISTYL 265-270; ASN_GLYCOSYLATION 9-12; CK2_PHOSPHO_SITE 77-80; ASN_GLYCOSYLATION 157-160; PKC_PHOSPHO_SITE 39-41; PKC_PHOSPHO_SITE 193-195;	MASPIN 180-195; SERPIN 86-433; MASPIN 201-215; MASPIN 251-264; MASPIN 319-331; MASPIN 387- 405; SERPIN 406-416; serpin 80-433; MASPIN 342-360;
DEX0450- 009.aa.1	N	1 - ol- 393;tm394 - 416;i417-	355-374,1.115; 341- 353,1.232; 391-422,1.231; 18-34,1.218; 117-134,1.11; 81-104,1.19; 37-50,1.233;	MYRISTYL 244-249; PKC_PHOSPHO_SITE 678-680; PKC_PHOSPHO_SITE 578-580; MYRISTYL 530-535; MYRISTYL 467-472; PKC_PHOSPHO_SITE 95-97;	

		705;	<p>500-511,1.095; 607-617,1.17; 622-644,1.18; 518-547,1.166; 551-579,1.243; 158-190,1.213; 54-72,1.198; 139-147,1.061; 306-319,1.186; 247-270,1.13; 667-702,1.182; 192-204,1.118; 276-299,1.146; 455-463,1.17; 588-598,1.073; 233-239,1.076; 425-444,1.136; 207-221,1.189; 485-491,1.077; 378-389,1.136;</p>	<p>PKC_PHOSPHO_SITE 169-171; CK2_PHOSPHO_SITE 108-111; ASN_GLYCOSYLATION 385-388; MYRISTYL 468-473; CK2_PHOSPHO_SITE 302-305; PKC_PHOSPHO_SITE 495-497; MYRISTYL 306-311; CK2_PHOSPHO_SITE 6-9; PKC_PHOSPHO_SITE 11-13; PKC_PHOSPHO_SITE 372-374; PKC_PHOSPHO_SITE 599-601; MYRISTYL 583-588; MYRISTYL 565-570; PKC_PHOSPHO_SITE 644-646; MYRISTYL 572-577; TYR_PHOSPHO_SITE 680-687; PKC_PHOSPHO_SITE 289-291; PKC_PHOSPHO_SITE 256-258; TYR_PHOSPHO_SITE 648-654; CK2_PHOSPHO_SITE 360-363; PKC_PHOSPHO_SITE 323-325; MYRISTYL 213-218; ASN_GLYCOSYLATION 638-641; PKC_PHOSPHO_SITE 510-512; MYRISTYL 520-525; CK2_PHOSPHO_SITE 603-606; PKC_PHOSPHO_SITE 482-484; MYRISTYL 694-699; CK2_PHOSPHO_SITE 640-643; PKC_PHOSPHO_SITE 107-109;</p>		
DEX0450-009.orf.1	N	<p>5 - ol-30;tm31-50;i51-61;tm62-84;o85-98;tm99-121;i122-122;tm123-145;o146-154;tm155-177;i178-226;</p>	<p>4-20,1.213; 182-198,1.119; 65-87,1.16; 31-37,1.082; 95-107,1.223; 39-51,1.222; 209-222,1.106; 148-177,1.21; 109-146,1.134;</p>	<p>MYRISTYL 32-37; MYRISTYL 121-126; PKC_PHOSPHO_SITE 22-24; MYRISTYL 107-112; CK2_PHOSPHO_SITE 87-90; MYRISTYL 110-115; CK2_PHOSPHO_SITE 220-223;</p>	<p>DUF6 41-173;</p>	

DEX0450- 009.aa.2	N	<p>10 - i1- 68;tm69- 86;o87- 100;tm101 - 120;i121- 239;tm240 - 262;o263- 266;tm267 - 289;i290- 295;tm296 - 318;o319- 327;tm328 - 347;i348- 358;tm359 - 381;o382- 395;tm396 - 418;i419- 419;tm420 - 442;o443- 451;tm452 - 474;i475- 570;</p> <p>406-443,1.134; 217- 235,1.075; 29-40,1.053; 479-495,1.119; 146- 151,1.087; 445-474,1.21; 71-96,1.26; 515-526,1.172; 42-53,1.213; 135-141,1.058; 544-563,1.229; 392- 404,1.223; 109-121,1.18; 528-536,1.067; 12-27,1.114; 191-197,1.025; 328- 334,1.082; 202-214,1.108; 161-176,1.18; 237- 261,1.173; 336-348,1.222; 264-290,1.179; 500- 513,1.117; 362-384,1.16; 298-317,1.213;</p>	<p>MYRISTYL 404-409; PKC_PHOSPHO_SITE 505-507; MYRISTYL 407-412; PKC_PHOSPHO_SITE 319-321; PKC_PHOSPHO_SITE 188-190; PKC_PHOSPHO_SITE 175-177; ASN GLYCOSYLATION 255-258; MYRISTYL 537-542; CK2_PHOSPHO_SITE 159-162; CK2_PHOSPHO_SITE 384-387; PKC_PHOSPHO_SITE 26-28; CK2_PHOSPHO_SITE 257-260; PKC_PHOSPHO_SITE 64-66; CK2_PHOSPHO_SITE 181-184; ASN GLYCOSYLATION 157-160; MYRISTYL 418-423; MYRISTYL 329-334; MYRISTYL 14-19; PKC_PHOSPHO_SITE 185-187;</p>	<p>DUF6 338-470;</p>
DEX0450- 010.aa.1	N	<p>119-132,1.08; 82-97,1.201; 100-106,1.044; 68-79,1.102; 30-56,1.184;</p>	<p>AMIDATION 124-127; CK2_PHOSPHO_SITE 25-28; CAMP_PHOSPHO_SITE 107-110; MYRISTYL 82-87; PKC_PHOSPHO_SITE 63- 65; ASN GLYCOSYLATION 115-118;</p>	
DEX0450	N	<p>67-79,1.128; 56-65,1.103;</p>	<p>CK2_PHOSPHO_SITE 7-10;</p>	

010.aa.2	82;	21-31,1.209; 8-19,1.146; 44-54,1.222;			
DEX0450- 010.orf. 2	0 - 01- 146; N	69-95,1.184; 107-118,1.102; 121-136,1.201; 8-20,1.101; 27-39,1.162;		PKC_PHOSPHO_SITE 102-104; MYRISTYL 121-126; MYRISTYL 7-12; MYRISTYL 19- 24; CK2_PHOSPHO_SITE 64-67; CK2_PHOSPHO_SITE 153-156; CK2_PHOSPHO_SITE 389-392; CAMP_PHOSPHO_SITE 384-387; MYRISTYL 102-107; ASN_GLYCOSYLATION 53-56; CAMP_PHOSPHO_SITE 63-66; CK2_PHOSPHO_SITE 142-145; PKC_PHOSPHO_SITE 142-144; CK2_PHOSPHO_SITE 603-606; MYRISTYL 270-275; AMIDATION 61-64; MYRISTYL 59-74; CK2_PHOSPHO_SITE 5-8; PKC_PHOSPHO_SITE 285-287; MYRISTYL 98-103; MYRISTYL 267-272; PKC_PHOSPHO_SITE 590-592; 71-76; CK2_PHOSPHO_SITE 75-78; TYR_PHOSPHO_SITE 442-448; MYRISTYL 103-108; CK2_PHOSPHO_SITE 76-79; PKC_PHOSPHO_SITE 603-605; CK2_PHOSPHO_SITE 182-185; CK2_PHOSPHO_SITE 314-317; PKC_PHOSPHO_SITE 525-527; CK2_PHOSPHO_SITE 188-191; PKC_PHOSPHO_SITE 459-461; CK2_PHOSPHO_SITE 239-242;	Rhodanese 458-566; RHOD 455-569; RHODANESE_3 465-572; MPIPHPTASE 588-606; MPIPHPTASE 571-588; MPIPHPTASE 431-448; MPIPHPTASE 471-491; MPIPHPTASE 513-533; MPIPHPTASE 543-564; MPIPHPTASE 449-469;
DEX0450- 010.aa.3	0 - 01- 614; N	39-53,1.134; 343-355,1.139; 605-611,1.097; 432- 442,1.137; 445-450,1.068; 85-93,1.063; 130-140,1.059; 401-414,1.106; 543- 558,1.125; 169-183,1.109; 300-312,1.176; 287- 292,1.051; 357-370,1.15; 316-322,1.026; 452- 460,1.094; 17-25,1.055; 223-240,1.138; 117- 124,1.081; 498-524,1.221; 154-162,1.105; 194- 219,1.141; 562-574,1.075; 463-479,1.176; 486- 492,1.099; 101-115,1.085; 326-335,1.168;		MYRISTYL 66-71; TYR_PHOSPHO_SITE 241-247; PKC_PHOSPHO_SITE 324-326; PKC_PHOSPHO_SITE 258-260; PKC_PHOSPHO_SITE 389-391; PKC_PHOSPHO_SITE 84-86; MYRISTYL 69- 74; CK2_PHOSPHO_SITE 402-405; CAMP_PHOSPHO_SITE 183-186; CK2_PHOSPHO_SITE 38-41;	MPIPHPTASE 312-332; MPIPHPTASE 387-405; MPIPHPTASE 370-387; MPIPHPTASE 342-363; MPIPHPTASE 270-290; Rhodanese 257-365; MPIPHPTASE 230-247; MPIPHPTASE 248-268;
DEX0450- 010.orf. 3	0 - 01- 413; N	200-213,1.106; 361- 373,1.075; 142-154,1.139; 156-169,1.15; 285- 291,1.099; 297-323,1.221; 99-111,1.176; 244- 249,1.068; 404-410,1.097; 29-39,1.138; 262-278,1.176; 231-241,1.137; 86-91,1.051;			

				4-19, 1.118; 251-259, 1.094; 342-357, 1.125; 115- 121, 1.026; 125-134, 1.168;	CK2_PHOSPHO_SITE 113-116; CK2_PHOSPHO_SITE 188-191; PKC_PHOSPHO_SITE 402-404;	RHOD 254-368; RHODANESE_3 264-371;
DEX0450- 011.aa.1	N	0 - ol- 331;		5-21, 1.1; 323-328, 1.063; 193-199, 1.131; 68-75, 1.118; 215-226, 1.064; 236- 257, 1.142; 267-283, 1.128; 297-304, 1.121; 25-38, 1.149; 160-168, 1.125; 108- 118, 1.147; 311-320, 1.098; 122-135, 1.132; 175- 186, 1.11; 81-87, 1.12; 49- 65, 1.181; 99-106, 1.048;	CAMP_PHOSPHO_SITE 42-45; CK2_PHOSPHO_SITE 284-287; MYRISTYL 55-60; CK2_PHOSPHO_SITE 78-81; CK2_PHOSPHO_SITE 232-235; PKC_PHOSPHO_SITE 154-156; MYRISTYL 101-106; CK2_PHOSPHO_SITE 222-225; PKC_PHOSPHO_SITE 232-234; CK2_PHOSPHO_SITE 88-91; CK2_PHOSPHO_SITE 240-243; PKC_PHOSPHO_SITE 311-313; PKC_PHOSPHO_SITE 116-118; MYRISTYL 298-303; PKC_PHOSPHO_SITE 226-228; CK2_PHOSPHO_SITE 163-166; MYRISTYL 202-207; MYRISTYL 308-313; PKC_PHOSPHO_SITE 120-122; CK2_PHOSPHO_SITE 176-179; PKC_PHOSPHO_SITE 295-297; AMIDATION 40-43; CAMP_PHOSPHO_SITE 229-232; CK2_PHOSPHO_SITE 302-305;	PH 5-106; PH 5-104; DEP 139-225; PH_DOMAIN_2 247-331; DEP 139-225; PH_DOMAIN_1 4-104; PH 248-330; DEP 139-225;
DEX0450- 012.aa.1	N	0 - ol- 176;		101-112, 1.097; 117- 142, 1.156; 48-76, 1.092; 82- 98, 1.105; 17-23, 1.144;	PKC_PHOSPHO_SITE 116-118; MYRISTYL 148-153; MYRISTYL 9-14; CK2_PHOSPHO_SITE 152-155; CK2_PHOSPHO_SITE 141-144;	PROTEASOME_PROTEASE 7- 158; PROTEASOME B 12- 59; proteasome 5-174;
DEX0450- 012.aa.2	N	0 - ol- 158;		117-142, 1.156; 48-76, 1.092; 17-23, 1.144; 82-98, 1.105; 101-112, 1.097;	CK2_PHOSPHO_SITE 141-144; PKC_PHOSPHO_SITE 116-118; MYRISTYL 9-14;	PROTEASOME_B 12-59; PROTEASOME_PROTEASE 7- 141; proteasome 5-153;
DEX0450- 013.aa.1	N	0 - ol- 246;		47-63, 1.144; 201-224, 1.153; 113-142, 1.174; 4-22, 1.133; 174-189, 1.118; 153- 159, 1.123; 65-107, 1.225; 27-38, 1.2; 165-170, 1.05;	MYRISTYL 239-244; PKC_PHOSPHO_SITE 47-49; PKC_PHOSPHO_SITE 83-85; CK2_PHOSPHO_SITE 62-65; MYRISTYL 202-207; CK2_PHOSPHO_SITE 190-193; CK2_PHOSPHO_SITE 212-215; MYRISTYL 41-46; CK2_PHOSPHO_SITE 111-114; PKC_PHOSPHO_SITE 62-64;	Tryp_SPC 20-214; trypsin 9-214; CHYMOTRYPSIN 164-176; TRYPSIN_SER 165-176; CHYMOTRYPSIN 66-80; TRYPSIN_DOM 31-219;

DEX0450- 014.aa.1	N	0 - 01- 273;	25-54, 1.089; 83-94, 1.124; 146-156, 1.098; 227- 235, 1.055; 68-75, 1.096; 197-208, 1.088; 259- 267, 1.184; 114-125, 1.067; 173-179, 1.088;	MYRISTYL 141-146; PKC_PHOSPHO_SITE 167-169; MYRISTYL 127-132; PKC_PHOSPHO_SITE 56-58; MYRISTYL 166-171; MYRISTYL 114-119; ASN_GLYCOSYLATION 101-104; PKC_PHOSPHO_SITE 251-253; MYRISTYL 244-249; ASN_GLYCOSYLATION 19-22; MYRISTYL 213-218; CK2_PHOSPHO_SITE 21-24; MYRISTYL 209-214; MYRISTYL 11-16; PKC_PHOSPHO_SITE 240-242; PKC_PHOSPHO_SITE 15-17; CAMP_PHOSPHO_SITE 269-272; MYRISTYL 161-166;	PRICHEXTENSIN 39-55; PRICHEXTENSIN 72-84; PRO_RICH 23-117; PRICHEXTENSIN 171-188;
DEX0450- 014.orf. 1	N	0 - 01- 278;	178-184, 1.088; 151- 161, 1.098; 264-272, 1.184; 202-213, 1.088; 119- 130, 1.067; 88-99, 1.124; 73- 80, 1.096; 4-9, 1.097; 232- 240, 1.055; 30-59, 1.089;	MYRISTYL 171-176; MYRISTYL 166-171; MYRISTYL 249-254; PKC_PHOSPHO_SITE 256-258; PKC_PHOSPHO_SITE 20-22; MYRISTYL 132-137; ASN_GLYCOSYLATION 106-109; MYRISTYL 119-124; PKC_PHOSPHO_SITE 172-174; ASN_GLYCOSYLATION 24-27; MYRISTYL 218-223; MYRISTYL 16-21; MYRISTYL 146-151; CK2_PHOSPHO_SITE 26-29; PKC_PHOSPHO_SITE 61-63; MYRISTYL 214-219; CAMP_PHOSPHO_SITE 274-277; PKC_PHOSPHO_SITE 245-247;	PRICHEXTENSIN 176-193; PRICHEXTENSIN 44-60; PRO_RICH 28-122; PRICHEXTENSIN 77-89;
DEX0450- 015.aa.1	N	0 - 01- 2306;	105-119, 1.087; 1545- 1561, 1.111; 1820- 1826, 1.106; 995-1002, 1.103; 609-616, 1.164; 1181- 1198, 1.154; 746-765, 1.113; 2079-2085, 1.046; 470- 476, 1.09; 4-15, 1.104; 346- 357, 1.136; 1296-1303, 1.105; 545-563, 1.195; 2018- 2027, 1.111; 1247- 1253, 1.094; 1663-	CK2_PHOSPHO_SITE 1853-1856; MYRISTYL 197-202; PKC_PHOSPHO_SITE 1480-1482; AMIDATION 1644-1647; CK2_PHOSPHO_SITE 1727-1730; PKC_PHOSPHO_SITE 166-168; CK2_PHOSPHO_SITE 1772-1775; CK2_PHOSPHO_SITE 2212-2215; CK2_PHOSPHO_SITE 2235-2238; CK2_PHOSPHO_SITE 1747-1750; PKC_PHOSPHO_SITE 1954-1956; MYRISTYL 250-255; PKC_PHOSPHO_SITE 806-808;	CPSASE 554-566; MGS 1315-1428; Amidohydro_1 1462-1695; CPSASE 434- 444; GATase 179-356; OTCace 2151-2303; CPSase_L_D3 798-921; CPSase_L_D2 1047-1268; AOTCACE 2050-2069; ANTSENTHASEII 332-345; AOTCACE 2268-2291; CPSase L D2 514-745;

		<p>1708,1.207; 809-830,1.186; 1639-1645,1.106; 2165- 2191,1.211; 1928- 1937,1.088; 1255-1281,1.2; 387-407,1.129; 1389- 1395,1.108; 1327-1349,1.14; 2135-2142,1.098; 2089- 2125,1.236; 855-872,1.134; 1200-1207,1.085; 156- 169,1.156; 2295-2303,1.167; 2270-2277,1.094; 1789- 1799,1.167; 1497- 1503,1.089; 1861- 1885,1.168; 874-910,1.171; 324-340,1.129; 176- 197,1.161; 70-76,1.077; 1371-1384,1.085; 1354- 1365,1.132; 1565- 1575,1.145; 1313- 1320,1.087; 1895- 1906,1.129; 415-423,1.07; 1010-1016,1.084; 688- 721,1.164; 526-532,1.078; 245-265,1.175; 199- 212,1.148; 1406-1412,1.084; 214-220,1.07; 1458- 1475,1.178; 226-242,1.154; 296-312,1.048; 1760- 1772,1.147; 777-782,1.049; 729-743,1.229; 1955- 1960,1.056; 629-638,1.153; 1828-1836,1.115; 437- 444,1.065; 1941-1947,1.028; 446-463,1.158; 645- 672,1.152; 1051-1058,1.071; 2281-2286,1.047; 2069- 2076,1.101; 1843-</p>	<p>CK2_PHOSPHO_SITE 1913-1916; MYRISTYL 2149-2154; CK2_PHOSPHO_SITE 2087- 2090; PKC_PHOSPHO_SITE 1458-1460; CK2_PHOSPHO_SITE 830-833; TYR_PHOSPHO_SITE 595-602; PKC_PHOSPHO_SITE 1863-1865; MYRISTYL 284-289; MYRISTYL 2153-2158; CK2_PHOSPHO_SITE 798-801; PKC_PHOSPHO_SITE 1953-1955; PKC_PHOSPHO_SITE 163-165; CK2_PHOSPHO_SITE 1829-1832; PKC_PHOSPHO_SITE 1606-1608; TYR_PHOSPHO_SITE 1333-1340; MYRISTYL 471-476; MYRISTYL 18-23; PKC_PHOSPHO_SITE 1331-1333; MICROBODIES_CTER 2304-2306; CK2_PHOSPHO_SITE 504-507; MYRISTYL 14-19; CK2_PHOSPHO_SITE 1294-1297; MYRISTYL 1550-1555; PKC_PHOSPHO_SITE 1415-1417; ASN_GLYCOSYLATION 1324- 1327; PKC_PHOSPHO_SITE 1396-1398; ASN_GLYCOSYLATION 141-144; MYRISTYL 142-147; CK2_PHOSPHO_SITE 761-764; MYRISTYL 184-189; MYRISTYL 1658- 1663; CK2_PHOSPHO_SITE 804-807; CK2_PHOSPHO_SITE 369-372; MYRISTYL 1659-1664; MYRISTYL 1681-1686; CK2_PHOSPHO_SITE 569-572; CK2_PHOSPHO_SITE 1379-1382; MYRISTYL 1924-1929; CK2_PHOSPHO_SITE 1805- 1808; MYRISTYL 1964-1969; CK2_PHOSPHO_SITE 1480-1483; MYRISTYL 1144-1149; CK2_PHOSPHO_SITE 1037- 1040; MYRISTYL 1712-1717; CK2_PHOSPHO_SITE 1360-1363; CK2_PHOSPHO_SITE 639-642; PKC_PHOSPHO_SITE 285-287;</p>	<p>CPSGATASE 289-300; PRO_RICH 1883-1997; CPSGATASE 264-281; CPSase_L_chain 392-512; AOTCACE_2133-2144; CPSase_L_chain 931- 1045; AOTCACE 2258- 2267; CPSaseII_lrg 388- 1440; CPSGATASE 214- 228; CPSASE_2 1212- 1219; CPSaseIIsma11 2- 359; CPSGATASE 247-263; ANTSNTHASEII 247-258; CPSASE_1 550-564; GATASE_TYPE_I 247-258; DIHYDROOROTASE_2 1765- 1776; CARBAMOYLTRANSFERASE 2050-2057; CPSASE_1 1083-1097; ATCACE 2040- 2062; DIHYDROOROTASE_1 1469-1477; CPSASE_2 680-687; ATCACE 2078- 2087; ATCACE 2262-2267; OTCace_N 2005-2148; ATCACE 2132-2149; ATCACE 2223-2232; GATASE 247-258; CPSASE 761-779; CPSase_sm_chain 1-151; CPSASE 623-640; CPSASE 680-709; ANTSNTHASEII 217-226; GATASE 217- 226; GATASE 332-345; CPSASE 405-419; ATCACE 2284-2298; CPSASE 588- 607; asd carb tr 2005-</p>
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1850,1.045; 1509- 1537,1.146; 1582- 1618,1.229; 1209-1241,1.18; 1108-1130,1.158; 429- 435,1.072; 1157-1171,1.092; 2239-2251,1.126; 33- 60,1.181; 481-505,1.141; 2060-2066,1.046; 79- 98,1.233; 17-31,1.094; 1134-1155,1.18; 376- 384,1.126; 1074-1095,1.237; 1988-2013,1.188; 1488- 1495,1.049; 1968- 1980,1.173; 601-607,1.093; 2219-2226,1.084; 131- 141,1.136; 574-593,1.155; 2195-2203,1.124; 1026- 1038,1.117; 1419-1456,1.19; 843-852,1.129; 1620- 1635,1.267; 676-686,1.125; 931-962,1.192; 1710- 1729,1.179; 2038- 2045,1.055; 277-292,1.178; 785-797,1.112; 2259- 2267,1.093; 146-152,1.106; 1806-1816,1.121; 914- 921,1.112;	PKC_PHOSPHO_SITE 2143-2145; MYRISTYL 132-137; PKC_PHOSPHO_SITE 266-268; PKC_PHOSPHO_SITE 872-874; MYRISTYL 485-490; PKC_PHOSPHO_SITE 2189-2191; ASN_GLYCOSYLATION 1560-1563; MYRISTYL 477-482; CK2_PHOSPHO_SITE 356-359; MYRISTYL 625-630; MYRISTYL 1010-1015; MYRISTYL 1017-1022; MYRISTYL 2070-2075; CK2_PHOSPHO_SITE 344-347; PKC_PHOSPHO_SITE 2195-2197; MYRISTYL 724-729; MYRISTYL 767-772; CK2_PHOSPHO_SITE 1069-1072; PKC_PHOSPHO_SITE 2181-2183; PKC_PHOSPHO_SITE 44-46; MYRISTYL 1095-1100; MYRISTYL 895-900; MYRISTYL 610-615; MYRISTYL 1546- 1551; CAMP_PHOSPHO_SITE 1403-1406; ASN_GLYCOSYLATION 1394-1397; MYRISTYL 564-569; CK2_PHOSPHO_SITE 771-774; CK2_PHOSPHO_SITE 1103-1106; CK2_PHOSPHO_SITE 1284-1287; CK2_PHOSPHO_SITE 2074-2077; PKC_PHOSPHO_SITE 369-371; MYRISTYL 1320-1325; CK2_PHOSPHO_SITE 981-984; MYRISTYL 562-567; AMIDATION 1401- 1404; CK2_PHOSPHO_SITE 947-950; PKC_PHOSPHO_SITE 1175-1177; MYRISTYL 80-85; MYRISTYL 1543-1548; MYRISTYL 1488-1493; CK2_PHOSPHO_SITE 924-927; PKC_PHOSPHO_SITE 752-754; MYRISTYL 1356-1361; PKC_PHOSPHO_SITE 1321- 1323; PKC_PHOSPHO_SITE 375-377; MYRISTYL 322-327; CK2_PHOSPHO_SITE 1562-1565; PKC_PHOSPHO_SITE 2054- 2056; PKC_PHOSPHO_SITE 125-127; PKC_PHOSPHO_SITE 1073-1075; TYR_PHOSPHO_SITE 2286-2293; MYRISTYL	2304; CPSGATASE 178- 192;
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146

				<p>1159-1164; PKC_PHOSPHO_SITE 929-931; MYRISTYL 216-221; PKC_PHOSPHO_SITE 793-795; CK2_PHOSPHO_SITE 2205-2208; CK2_PHOSPHO_SITE 23-26; PKC_PHOSPHO_SITE 569-571; PKC_PHOSPHO_SITE 2027-2029; MYRISTYL 363-368; PKC_PHOSPHO_SITE 593-595; PKC_PHOSPHO_SITE 356-358; CK2_PHOSPHO_SITE 103-106; MYRISTYL 318-323; CK2_PHOSPHO_SITE 2143-2146; MYRISTYL 1279-1284; MYRISTYL 1251-1256; MYRISTYL 561-566; MYRISTYL 403-408;</p>			
DEX0450 015.orf. 1	N	0 - 01- 1651;		<p>793-805,1.112; 78-84,1.077; 1018-1024,1.084; 384- 392,1.126; 534-540,1.078; 1628-1643,1.267; 164- 177,1.156; 617-624,1.164; 1321-1328,1.087; 1255- 1261,1.094; 922-929,1.112; 4-23,1.129; 1263-1289,1.2; 437-443,1.072; 851- 860,1.129; 737-751,1.229; 817-838,1.186; 1590- 1626,1.229; 882-918,1.171; 1496-1503,1.049; 684- 694,1.125; 395-415,1.129; 454-471,1.158; 184- 205,1.161; 304-320,1.048; 785-790,1.049; 207- 220,1.148; 87-106,1.233; 253-273,1.175; 609- 615,1.093; 754-773,1.113; 696-729,1.164; 1573- 1583,1.145; 1116- 1138,1.158; 1034- 1046,1.117; 234-250,1.154;</p>	<p>ASN GLYCOSYLATION 1402-1405; PKC_PHOSPHO_SITE 760-762; MYRISTYL 192-197; PKC_PHOSPHO_SITE 364-366; ASN GLYCOSYLATION 1568-1571; CK2_PHOSPHO_SITE 1488-1491; MYRISTYL 618-623; MYRISTYL 572-577; PKC_PHOSPHO_SITE 801-803; MYRISTYL 26-31; CK2_PHOSPHO_SITE 1387-1390; PKC_PHOSPHO_SITE 880-882; CK2_PHOSPHO_SITE 512-515; CK2_PHOSPHO_SITE 1570-1573; MYRISTYL 1496-1501; MYRISTYL 150-155; MYRISTYL 371-376; MYRISTYL 292-297; MYRISTYL 330-335; MYRISTYL 633-638; CK2_PHOSPHO_SITE 352-355; MYRISTYL 140-145; ASN GLYCOSYLATION 149-152; MYRISTYL 485-490; MYRISTYL 1558-1563; MYRISTYL 1554-1559; PKC_PHOSPHO_SITE 293-295; CK2_PHOSPHO_SITE 1045-1048; MYRISTYL 1551-1556; MYRISTYL 569-574; CK2_PHOSPHO_SITE 989-992; MYRISTYL 88-93; ASN GLYCOSYLATION 1332-1335; MYRISTYL 493-498; MYRISTYL 1025-</p>	<p>CPSASE 596-615; CPSGATASE 272-289; GATASE 255-266; CPSase_L_D3 806-929; CPSASE 769-787; CPSASE 442-452; GATASE_TYPE_I 255-266; GATASE 225-234; MGS 1323-1436; GATase 187-364; GATASE 340-353; CPSase_L_chain 400-520; CPSASE_1 1091-1105; CPSASE_1 558-572; CPSASE 562-574; DIHYDROROTASE_1 1477-1485; CPSASE 688-717; CPSASE 631-648; ANTSNTHASEII 225-234; CPSaseIISmall 10-367; CPSase_L_D2 1055-1276; CPSaseII_lrg 396-1448; CPSase_L_chain 939-1053; CPSase_L_D2 522-753; ANTSNTHASEII 340-353; CPSASE 2 1220-</p>	

		<p>637-646, 1.153; 139-149, 1.136; 582-601, 1.155; 553-571, 1.195; 332-348, 1.129; 1362-1373, 1.132; 653-680, 1.152; 1189-1206, 1.154; 354-365, 1.136; 1059-1066, 1.071; 1427-1464, 1.19; 1517-1545, 1.146; 863-880, 1.134; 1466-1483, 1.178; 1397-1403, 1.108; 939-970, 1.192; 25-39, 1.094; 1553-1569, 1.111; 1379-1392, 1.085; 285-300, 1.178; 1082-1103, 1.237; 41-68, 1.181; 1208-1215, 1.085; 1003-1010, 1.103; 489-513, 1.141; 113-127, 1.087; 478-484, 1.09; 1304-1311, 1.105; 445-452, 1.065; 154-160, 1.106; 1414-1420, 1.084; 1165-1179, 1.092; 222-228, 1.07; 423-431, 1.07; 1142-1163, 1.18; 1335-1357, 1.14; 1505-1511, 1.089; 1217-1249, 1.18;</p>	<p>1030; MYRISTYL 22-27; PKC_PHOSPHO_SITE 171-173; PKC_PHOSPHO_SITE 174-176; PKC_PHOSPHO_SITE 52-54; TYR_PHOSPHO_SITE 603-610; TYR_PHOSPHO_SITE 1341-1348; CK2_PHOSPHO_SITE 955-958; PKC_PHOSPHO_SITE 274-276; CK2_PHOSPHO_SITE 1302-1305; PKC_PHOSPHO_SITE 133-135; CK2_PHOSPHO_SITE 1292-1295; CK2_PHOSPHO_SITE 1111-1114; CK2_PHOSPHO_SITE 932-935; CK2_PHOSPHO_SITE 31-34; PKC_PHOSPHO_SITE 937-939; PKC_PHOSPHO_SITE 1614-1616; PKC_PHOSPHO_SITE 1423-1425; CK2_PHOSPHO_SITE 1077-1080; MYRISTYL 1259-1264; PKC_PHOSPHO_SITE 1329-1331; MYRISTYL 1287-1292; MYRISTYL 1328-1333; MYRISTYL 479-484; PKC_PHOSPHO_SITE 1183-1185; MYRISTYL 1167-1172; CK2_PHOSPHO_SITE 806-809; PKC_PHOSPHO_SITE 1081-1083; PKC_PHOSPHO_SITE 1488-1490; CK2_PHOSPHO_SITE 111-114; CK2_PHOSPHO_SITE 779-782; AMIDATION 1409-1412; CK2_PHOSPHO_SITE 377-380; CAMP_PHOSPHO_SITE 1411-1414; MYRISTYL 258-263; CK2_PHOSPHO_SITE 1368-1371; PKC_PHOSPHO_SITE 1404-1406; MYRISTYL 205-210; PKC_PHOSPHO_SITE 1466-1468; PKC_PHOSPHO_SITE 383-385; MYRISTYL 732-737; MYRISTYL 224-229; CK2_PHOSPHO_SITE 577-580; PKC_PHOSPHO_SITE 377-379;</p>	<p>1227; CPSase_sm_chain 8-159; ANTSNTHASEII 255-266; CPSASE_2 688-695; CPSGATASE 222-236; CPSGATASE 255-271; CPSGATASE 186-200; CPSGATASE 297-308; CPSASE 413-427;</p>
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				CK2_PHOSPHO_SITE 364-367; CK2_PHOSPHO_SITE 812-815; PKC_PHOSPHO_SITE 1339-1341; MYRISTYL 411-416; CK2_PHOSPHO_SITE 838-841; PKC_PHOSPHO_SITE 577-579; MYRISTYL 775-780; CK2_PHOSPHO_SITE 647-650; MYRISTYL 1103-1108; MYRISTYL 1018- 1023; PKC_PHOSPHO_SITE 814-816; CK2_PHOSPHO_SITE 769-772; MYRISTYL 1152-1157; MYRISTYL 1364-1369; MYRISTYL 570-575; PKC_PHOSPHO_SITE 601-603; MYRISTYL 903-908; MYRISTYL 326-331;		
DEX0450- 015.aa.2	N	0 - 01- 2242;	1209-1241,1.18; 1679- 1691,1.147; 1181- 1198,1.154; 437-444,1.065; 33-60,1.181; 574-593,1.155; 2131-2139,1.124; 245- 265,1.175; 809-830,1.186; 70-76,1.077; 199-212,1.148; 1974-1981,1.055; 2071- 2078,1.098; 645-672,1.152; 629-638,1.153; 1134- 1155,1.18; 214-220,1.07; 481-505,1.141; 1780- 1804,1.168; 1725- 1735,1.121; 874-910,1.171; 1565-1575,1.145; 156- 169,1.156; 446-463,1.158; 526-532,1.078; 1904- 1916,1.173; 1488- 1495,1.049; 470-476,1.09; 688-721,1.164; 429- 435,1.072; 1010-1016,1.084; 176-197,1.161; 1924- 1949,1.188; 2217- 2222,1.047; 2005-	CK2_PHOSPHO_SITE 798-801; CK2_PHOSPHO_SITE 830-833; MYRISTYL 1543-1548; MICROBODIES_CTER 2240- 2242; MYRISTYL 1488-1493; CK2_PHOSPHO_SITE 924-927; PKC_PHOSPHO_SITE 1480-1482; PKC_PHOSPHO_SITE 163-165; CK2_PHOSPHO_SITE 639-642; MYRISTYL 2089-2094; CK2_PHOSPHO_SITE 569-572; PKC_PHOSPHO_SITE 266-268; CK2_PHOSPHO_SITE 1832-1835; MYRISTYL 284-289; CK2_PHOSPHO_SITE 369-372; MYRISTYL 1356-1361; CK2_PHOSPHO_SITE 771-774; MYRISTYL 2085-2090; PKC_PHOSPHO_SITE 166-168; CK2_PHOSPHO_SITE 1772-1775; CK2_PHOSPHO_SITE 761-764; PKC_PHOSPHO_SITE 1990-1992; AMIDATION 1401-1404; CK2_PHOSPHO_SITE 2010-2013; PKC_PHOSPHO_SITE 1458-1460; PKC_PHOSPHO_SITE 1963-1965; CK2_PHOSPHO_SITE 2023-2026; PKC PHOSPHO SITE 2079-2081;	DIHYDROOROTASE_1 1469- 1477; ATCASE 2220-2234; GATASE_TYPE_I 247-258; ATCASE 2198-2203; CPSase_L_chain 931- 1045; ANTSENTHASEII 247- 258; CPSASE_1 550-564; CPSASE 554-566; CPSASE 434-444; CPSASE 623- 640; CPSase_L_D2 1047- 1268; CPSase_L_D2 514- 745; AOTCASE 1986-2005; CPSASE 588-607; AOTCASE 2204-2227; AOTCASE 2194-2203; AOTCASE 2069-2080; GATase 179- 356; CPSase_L_chain 392-512; MGS 1315-1428; CARBAMOYLTRANSFERASE 1986-1993; Amidohydro_1 1462-1694; DIHYDROOROTASE_2 1684- 1695; GATASE 217-226; CPSase L D3 798-921;	

		<p>2012,1.101; 676-686,1.125; 415-423,1.07; 1074- 1095,1.237; 2231- 2239,1.167; 1762- 1769,1.045; 1051- 1058,1.071; 1996- 2002,1.046; 324-340,1.129; 1847-1856,1.088; 1509- 1537,1.146; 1814- 1825,1.129; 1497- 1503,1.089; 79-98,1.233; 226-242,1.154; 105- 119,1.087; 1891-1896,1.056; 1708-1718,1.167; 2025- 2061,1.236; 777-782,1.049; 1860-1871,1.139; 1354- 1365,1.132; 131-141,1.136; 1026-1038,1.117; 4- 15,1.104; 1255-1281,1.2; 2155-2162,1.084; 914- 921,1.112; 1327-1349,1.14; 746-765,1.113; 387- 407,1.129; 1371-1384,1.085; 1739-1745,1.106; 1200- 1207,1.085; 729-743,1.229; 346-357,1.136; 855- 872,1.134; 545-563,1.195; 2015-2021,1.046; 1313- 1320,1.087; 785-797,1.112; 296-312,1.048; 1545- 1561,1.111; 1296- 1303,1.105; 2101- 2127,1.211; 1389- 1395,1.108; 376-384,1.126; 1747-1755,1.115; 843- 852,1.129; 1247-1253,1.094; 1629-1648,1.179; 1582-</p>	<p>CK2_PHOSPHO_SITE 1562-1565; MYRISTYL 1900-1905; CK2_PHOSPHO_SITE 1480- 1483; MYRISTYL 322-327; MYRISTYL 363-368; CK2_PHOSPHO_SITE 1379-1382; PKC_PHOSPHO_SITE 369-371; CK2_PHOSPHO_SITE 2079-2082; MYRISTYL 1144-1149; ASN_GLYCOSYLATION 1394- 1397; MYRISTYL 318-323; CK2_PHOSPHO_SITE 1748-1751; PKC_PHOSPHO_SITE 375-377; MYRISTYL 1320-1325; CK2_PHOSPHO_SITE 1666- 1669; MYRISTYL 197-202; MYRISTYL 1251-1256; CK2_PHOSPHO_SITE 804-807; MYRISTYL 1159-1164; CK2_PHOSPHO_SITE 1646-1649; CK2_PHOSPHO_SITE 1037- 1040; MYRISTYL 1279-1284; CK2_PHOSPHO_SITE 2171-2174; MYRISTYL 184-189; CK2_PHOSPHO_SITE 2148-2151; MYRISTYL 1095-1100; MYRISTYL 216- 221; CK2_PHOSPHO_SITE 947-950; CK2_PHOSPHO_SITE 2141-2144; 1010-1015; TYR_PHOSPHO_SITE 595-602; MYRISTYL 250-255; ASN_GLYCOSYLATION 1560-1563; MYRISTYL 1017-1022; MYRISTYL 767-772; PKC_PHOSPHO_SITE 872-874; MYRISTYL 471-476; MYRISTYL 561-566; PKC_PHOSPHO_SITE 793-795; TYR_PHOSPHO_SITE 1333-1340; CK2_PHOSPHO_SITE 1069-1072; PKC_PHOSPHO_SITE 1175-1177; CK2_PHOSPHO_SITE 1294-1297; MYRISTYL 724-729; MYRISTYL 477-482; MYRISTYL 18-23; MYRISTYL 403-408; ASN_GLYCOSYLATION 1324-1327; MYRISTYL 80-85; MYRISTYL 14-19; ASN_GLYCOSYLATION 141-144; MYRISTYL</p>	<p>GATASE 247-258; CPSASE 680-709; CPSase_sm_chain 1-151; OTCace 2087-2239; OTCace_N 1941-2084; CPSASE 761-779; CPSGATASE 247-263; CPSASE 405-419; CPSASE 2 1212-1219; ATCACE 2068-2085; ANTSNTHASEII 217-226; ANTSNTHASEII 332-345; CPSGATASE 264-281; ATCACE 2159-2168; CPSASE_1 1083-1097; CPSGATASE 178-192; CPSaseIIsmall 2-359; CPSGATASE 214-228; GATASE 332-345; ATCACE 1976-1998; asp_carb tir 1941-2240; CPSaseII_lrg 388-1440; ATCACE 2014- 2023; CPSGATASE 289- 300; CPSASE 2 680-687; pyrC_multi 1425-1797;</p>
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DEX0450_015.aa.3	N	0 - ol-371;	134-141, 1.101; 125-131.1.046; 53-78.1.188;	1618, 1.229; 1406-1412, 1.084; 2175-2187, 1.126; 1954-1963, 1.111; 1157-1171, 1.092; 1108-1130, 1.158; 609-616, 1.164; 1620-1627, 1.123; 17-31, 1.094; 931-962, 1.192; 1458-1475, 1.178; 995-1002, 1.103; 2206-2213, 1.094; 146-152, 1.106; 277-292, 1.178; 601-607, 1.093; 1419-1456, 1.19; 2195-2203, 1.093;	895-900; CK2_PHOSPHO_SITE 23-26; MYRISTYL 485-490; PKC_PHOSPHO_SITE 752-754; PKC_PHOSPHO_SITE 806-808; PKC_PHOSPHO_SITE 356-358; MYRISTYL 1873-1878; PKC_PHOSPHO_SITE 2131-2133; TYR_PHOSPHO_SITE 2222-2229; PKC_PHOSPHO_SITE 2117-2119; PKC_PHOSPHO_SITE 2125-2127; MYRISTYL 625-630; CK2_PHOSPHO_SITE 1691-1694; MYRISTYL 564-569; CK2_PHOSPHO_SITE 1724-1727; PKC_PHOSPHO_SITE 44-46; PKC_PHOSPHO_SITE 593-595; MYRISTYL 562-567; PKC_PHOSPHO_SITE 569-571; CK2_PHOSPHO_SITE 1284-1287; MYRISTYL 2006-2011; CK2_PHOSPHO_SITE 1103-1106; CK2_PHOSPHO_SITE 1360-1363; CAMP_PHOSPHO_SITE 1403-1406; CK2_PHOSPHO_SITE 103-106; MYRISTYL 610-615; CK2_PHOSPHO_SITE 356-359; PKC_PHOSPHO_SITE 1782-1784; PKC_PHOSPHO_SITE 1606-1608; PKC_PHOSPHO_SITE 1415-1417; MYRISTYL 1550-1555; PKC_PHOSPHO_SITE 1321-1323; PKC_PHOSPHO_SITE 1890-1892; MYRISTYL 1843-1848; MYRISTYL 1631-1636; PKC_PHOSPHO_SITE 929-931; CK2_PHOSPHO_SITE 344-347; PKC_PHOSPHO_SITE 1396-1398; MYRISTYL 132-137; MYRISTYL 142-147; MYRISTYL 1546-1551; CK2_PHOSPHO_SITE 504-507; PKC_PHOSPHO_SITE 125-127; PKC_PHOSPHO_SITE 1889-1891; PKC_PHOSPHO_SITE 1331-1333; PKC_PHOSPHO_SITE 285-287; PKC_PHOSPHO_SITE 1073-1075;	ATCASE 105-127; AOTCASE 333-356;
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			<p>346-351,1.047; 144-150,1.046; 230-256,1.211; 154-190,1.236; 33-45,1.173; 335-342,1.094; 360-368,1.167; 20-25,1.056; 4-11,1.239; 103-110,1.055; 324-332,1.093; 260-268,1.124; 304-316,1.126; 284-291,1.084; 83-92,1.111; 200-207,1.098;</p>	<p>218-223; MYRISTYL 29-34; PKC_PHOSPHO_SITE 18-20; PKC_PHOSPHO_SITE 19-21; CK2_PHOSPHO_SITE 270-273; CK2_PHOSPHO_SITE 208-211; PKC_PHOSPHO_SITE 246-248; MYRISTYL 135-140; MYRISTYL 214-219; PKC_PHOSPHO_SITE 208-210; PKC_PHOSPHO_SITE 92-94; CK2_PHOSPHO_SITE 152-155; MICROBODIES_CTER 369-371; TYR_PHOSPHO_SITE 351-358; CK2_PHOSPHO_SITE 139-142; PKC_PHOSPHO_SITE 260-262; PKC_PHOSPHO_SITE 119-121; CK2_PHOSPHO_SITE 277-280;</p>	<p>CARBAMOYLTRANSFERASE 115-122; ATCase 143-152; ATCase 349-363; ATCase 327-332; OTCase 347-358; AOTCase 323-332; OTCase 113-127; ATCase 197-214; AOTCase 198-209; AOTCase 115-134; OTCase 146-159; OTCase 216-368; ATCase 288-297; OTCase_N 70-213; asp_carb_tr 70-369;</p>
DEX0450-016.aa.1	N	0 - ol-970;	<p>83-104,1.166; 449-555,1.169; 265-270,1.091; 590-600,1.164; 742-757,1.14; 348-358,1.081; 329-339,1.103; 412-421,1.054; 814-822,1.096; 202-210,1.06; 4-20,1.147; 219-234,1.083; 424-446,1.104; 905-940,1.173; 623-671,1.144; 160-167,1.132; 174-180,1.083; 280-297,1.246; 305-320,1.128; 570-581,1.068; 111-119,1.128; 602-619,1.152; 711-725,1.166; 885-898,1.133; 39-61,1.134; 239-255,1.136; 402-409,1.095; 845-863,1.146; 184-191,1.084; 943-948,1.023; 128-151,1.174; 385-399,1.15; 790-</p>	<p>MYRISTYL 40-45; CK2_PHOSPHO_SITE 25-28; CAMP_PHOSPHO_SITE 729-732; CAMP_PHOSPHO_SITE 190-193; MYRISTYL 194-199; CK2_PHOSPHO_SITE 27-30; CK2_PHOSPHO_SITE 235-238; PKC_PHOSPHO_SITE 33-35; MYRISTYL 902-907; LEUCINE_ZIPPER 821-842; CAMP_PHOSPHO_SITE 768-771; CK2_PHOSPHO_SITE 261-264; CAMP_PHOSPHO_SITE 258-261; PKC_PHOSPHO_SITE 672-674; MYRISTYL 7-12; PKC_PHOSPHO_SITE 762-764; CK2_PHOSPHO_SITE 23-26; CK2_PHOSPHO_SITE 725-728; ASN_GLYCOSYLATION 763-766; CK2_PHOSPHO_SITE 672-675; PKC_PHOSPHO_SITE 497-499; CK2_PHOSPHO_SITE 625-628; PKC_PHOSPHO_SITE 936-938; AMIDATION 687-690; PKC_PHOSPHO_SITE 103-105; PKC PHOSPHO SITE 98-100; MYRISTYL</p>	<p>HLH_2 766-822; PRICHEXTENSIN 449-470; PRO_RICH 374-671; HLH 773-827; HLH 768-822; PRICHEXTENSIN 378-394; PRICHEXTENSIN 470-486; PRICHEXTENSIN 506-531; HLH_1 806-821;</p>

DEX0450- 016.orf. 1	Y	0 - ol- 719;	810, 1.126;	715-720; PKC_PHOSPHO_SITE 802-804; PKC_PHOSPHO_SITE 564-566; CAMP_PHOSPHO_SITE 137-140; CK2_PHOSPHO_SITE 357-360; MYRISTYL 3-8; MYRISTYL 792-797; PKC_PHOSPHO_SITE 745-747; PKC_PHOSPHO_SITE 911-913; MYRISTYL 857-862; PKC_PHOSPHO_SITE 727-729; MYRISTYL 695-700; CK2_PHOSPHO_SITE 621-624; CAMP_PHOSPHO_SITE 693-696; MYRISTYL 941-946;	
				CK2_PHOSPHO_SITE 253-256; MYRISTYL 25-30; PKC_PHOSPHO_SITE 51-53; CAMP_PHOSPHO_SITE 711-714; CK2_PHOSPHO_SITE 43-46; CK2_PHOSPHO_SITE 643-646; MYRISTYL 212-217; CK2_PHOSPHO_SITE 279-282; PKC_PHOSPHO_SITE 116-118; CK2_PHOSPHO_SITE 41-44; PKC_PHOSPHO_SITE 582-584; PKC_PHOSPHO_SITE 515-517; PKC_PHOSPHO_SITE 121-123; CK2_PHOSPHO_SITE 45-48; CAMP_PHOSPHO_SITE 208-211; MYRISTYL 21-26; MYRISTYL 58-63; CAMP_PHOSPHO_SITE 276-279; CK2_PHOSPHO_SITE 639-642; MYRISTYL 713-718; CK2_PHOSPHO_SITE 375-378; PKC_PHOSPHO_SITE 690-692; CK2_PHOSPHO_SITE 690-693; CAMP_PHOSPHO_SITE 155-158; AMIDATION 705-708;	
DEX0450- 016.aa.2	N	0 - ol- 629;	504-522, 1.146; 261- 278, 1.152; 449-469, 1.126; 602-607, 1.023; 473- 481, 1.096; 249-259, 1.164;	LEUCINE ZIPPER 480-501; PKC_PHOSPHO_SITE 595-597; PKC_PHOSPHO_SITE 19-21; PKC_PHOSPHO_SITE 331-333; MYRISTYL	PRICHEXTENS 396-412; PRICHEXTENS 488-504; PRICHEXTENS 467-488; PRO_RICH 392-689; PRICHEXTENS 524-549; PRICHEXTENS 165-190; PRICHEXTENS 112-128; HLH 2 425-481; PRICHEXTENS 33-45;

		<p>108-214, 1.169; 282-330, 1.144; 544-557, 1.133; 71-80, 1.054; 13-20, 1.057; 61-68, 1.095; 44-58, 1.15; 229-240, 1.068; 564-599, 1.173; 401-416, 1.14; 370-384, 1.166; 83-105, 1.104;</p>		<p>600-605; CAMP_PHOSPHO_SITE 388-391; PKC_PHOSPHO_SITE 386-388; CK2_PHOSPHO_SITE 280-283; CAMP_PHOSPHO_SITE 352-355; MYRISTYL 561-566; MYRISTYL 516-521; ASN_GLYCOSYLATION 422-425; PKC_PHOSPHO_SITE 404-406; AMIDATION 346-349; PKC_PHOSPHO_SITE 421-423; PKC_PHOSPHO_SITE 461-463; CAMP_PHOSPHO_SITE 427-430; PKC_PHOSPHO_SITE 570-572; MYRISTYL 12-17; PKC_PHOSPHO_SITE 223-225; CK2_PHOSPHO_SITE 331-334; MYRISTYL 451-456; CK2_PHOSPHO_SITE 284-287; CK2_PHOSPHO_SITE 384-387; PKC_PHOSPHO_SITE 156-158; MYRISTYL 374-379; MYRISTYL 354-359;</p>	<p>PRICHEXTENSIN 132-149; PRO_RICH 33-330; HLH_1 465-480; HLH 427-481; HLH 432-486;</p>
<p>DEX0450-016.crf.2</p>	<p>0 - 01-382; N</p>	<p>66-80, 1.15; 105-127, 1.104; 304-352, 1.144; 93-102, 1.054; 271-281, 1.164; 35-42, 1.057; 283-300, 1.152; 83-90, 1.095; 251-262, 1.068; 16-29, 1.151; 130-236, 1.169; 4-11, 1.133;</p>	<p>0 - 01-382; N</p>	<p>PKC_PHOSPHO_SITE 178-180; MYRISTYL 11-16; MYRISTYL 376-381; PKC_PHOSPHO_SITE 41-43; PKC_PHOSPHO_SITE 353-355; CK2_PHOSPHO_SITE 306-309; AMIDATION 368-371; CK2_PHOSPHO_SITE 353-356; MYRISTYL 34-39; MYRISTYL 14-19; MYRISTYL 15-20; CAMP_PHOSPHO_SITE 374-377; CK2_PHOSPHO_SITE 302-305; MYRISTYL 18-23; PKC_PHOSPHO_SITE 245-247;</p>	<p>PRICHEXTENSIN 146-171; PRICHEXTENSIN 54-71; CARBMTKINASE 77-92; PRO_RICH 55-352; CARBMTKINASE 3-21;</p>
<p>DEX0450-016.aa.3</p>	<p>0 - 01-1009; N</p>	<p>781-796, 1.14; 641-658, 1.152; 174-180, 1.083; 184-191, 1.084; 629-639, 1.164; 488-594, 1.169; 368-378, 1.103; 451-460, 1.054; 853-861, 1.096; 424-438, 1.15; 344-359, 1.128; 128-151, 1.174;</p>	<p>0 - 01-1009; N</p>	<p>CK2_PHOSPHO_SITE 300-303; PKC_PHOSPHO_SITE 784-786; CK2_PHOSPHO_SITE 664-667; PKC_PHOSPHO_SITE 801-803; MYRISTYL 194-199; MYRISTYL 734-739; CAMP_PHOSPHO_SITE 190-193; MYRISTYL 896-901; MYRISTYL 754-759; CAMP PHOSPHO SITE 297-300; MYRISTYL</p>	<p>HLH 812-866; HLH 807-861; PRO_RICH 413-710; HLH_2 805-861; HLH_1 845-860; PRICHEXTENSIN 509-525; PRICHEXTENSIN 417-433; PRICHEXTENSIN 545-570; PRICHEXTENSIN 488-509;</p>

			<p>982-987, 1.023; 944-979, 1.173; 83-104, 1.166; 609-620, 1.068; 662-710, 1.144; 319-336, 1.246; 219-234, 1.083; 111-119, 1.128; 39-61, 1.134; 387-397, 1.081; 924-937, 1.133; 239-263, 1.136; 202-210, 1.06; 160-167, 1.132; 441-448, 1.095; 285-298, 1.244; 829-849, 1.126; 265-271, 1.099; 463-485, 1.104; 304-309, 1.091; 884-902, 1.146; 750-764, 1.166; 4-20, 1.147;</p>	<p>831-836; CK2_PHOSPHO_SITE 27-30; LEUCINE_ZIPPER 860-881; CK2_PHOSPHO_SITE 711-714; MYRISTYL 941-946; CAMP_PHOSPHO_SITE 807-810; PKC_PHOSPHO_SITE 33-35; PKC_PHOSPHO_SITE 841-843; MYRISTYL 282-287; CK2_PHOSPHO_SITE 660-663; PKC_PHOSPHO_SITE 603-605; PKC_PHOSPHO_SITE 950-952; MYRISTYL 287-292; PKC_PHOSPHO_SITE 536-538; ASN_GLYCOSYLATION 802-805; CK2_PHOSPHO_SITE 23-26; MYRISTYL 980-985; MYRISTYL 3-8; PKC_PHOSPHO_SITE 103-105; CK2_PHOSPHO_SITE 235-238; CK2_PHOSPHO_SITE 25-28; MYRISTYL 7-12; PKC_PHOSPHO_SITE 98-100; CAMP_PHOSPHO_SITE 768-771; CK2_PHOSPHO_SITE 764-767; PKC_PHOSPHO_SITE 975-977; PKC_PHOSPHO_SITE 766-768; RGD 271-273; CK2_PHOSPHO_SITE 270-273; MYRISTYL 40-45; PKC_PHOSPHO_SITE 711-713; CAMP_PHOSPHO_SITE 137-140; CAMP_PHOSPHO_SITE 732-735; CK2_PHOSPHO_SITE 396-399; AMIDATION 726-729;</p>	<p>PRICHEXTENS 269-294; PRICHEXTENS 221-237; PRICHEXTENS 142-154; PRICHEXTENS 241-258; PRO_RICH 142-439;</p>
DEX0450-016.orf.3	N	0 - 01-469;	<p>391-439, 1.144; 73-88, 1.128; 338-349, 1.068; 192-214, 1.104; 180-189, 1.054; 153-167, 1.15; 170-177, 1.095; 48-65, 1.246; 358-368, 1.164; 217-323, 1.169; 33-38, 1.091; 16-27, 1.244; 116-126, 1.081; 370-387, 1.152; 97-107, 1.103;</p>	<p>CK2_PHOSPHO_SITE 125-128; AMIDATION 455-458; CAMP_PHOSPHO_SITE 461-464; PKC_PHOSPHO_SITE 440-442; MYRISTYL 463-468; PKC_PHOSPHO_SITE 332-334; PKC_PHOSPHO_SITE 265-267; CK2_PHOSPHO_SITE 29-32; CK2_PHOSPHO_SITE 393-396; CK2_PHOSPHO_SITE 440-443; MYRISTYL 16-21; CAMP_PHOSPHO_SITE 26-29; CK2_PHOSPHO_SITE 389-392;</p>	

DEX0450- 017.aa.1	N	0 - ol- 191;	4-25,1.16; 100-122,1.125; 146-158,1.049; 83-95,1.18; 67-73,1.11;	MYRISTYL 35-40; PKC_PHOSPHO_SITE 81-83; MYRISTYL 167-172; ASN_GLYCOSYLATION 79-82; MYRISTYL 164-169; MYRISTYL 78-83;	PRICHEXTENSIN 64-85; PRICHEXTENSIN 15-27;
DEX0450- 017.aa.2	N	0 - ol- 117;	49-84,1.09; 104-114,1.087;	MYRISTYL 42-47; MYRISTYL 93-98; MYRISTYL 22-27; MYRISTYL 32-37; MYRISTYL 90-95; MYRISTYL 2-7; MYRISTYL 12-17; MYRISTYL 50-55;	GLY_RICH 2-51;
DEX0450- 017.orf.2	N	0 - ol- 165;	157-162,1.028; 84-101,1.106; 112-135,1.165; 43-82,1.208; 103-109,1.036;	MYRISTYL 67-72; PKC_PHOSPHO_SITE 27-29; CK2_PHOSPHO_SITE 45-48; AMIDATION 148-151; CK2_PHOSPHO_SITE 7-10;	ATP_GTP_A 23-30;
DEX0450- 017.aa.3	N	0 - ol- 146;	113-121,1.125; 49-84,1.09;	MYRISTYL 22-27; MYRISTYL 108-113; MYRISTYL 90-95; MYRISTYL 93-98; MYRISTYL 32-37; MYRISTYL 42-47; MYRISTYL 106-111; MYRISTYL 12-17; MYRISTYL 50-55; MYRISTYL 2-7;	GLY_RICH 2-51;
DEX0450- 017.orf.3	N	0 - ol- 165;	103-109,1.036; 43-82,1.208; 157-162,1.028; 112-135,1.165; 84-101,1.106;	CK2_PHOSPHO_SITE 7-10; PKC_PHOSPHO_SITE 27-29; AMIDATION 148-151; CK2_PHOSPHO_SITE 45-48; MYRISTYL 67-72;	ATP_GTP_A 23-30;
DEX0450- 018.aa.1	Y	0 - ol- 636;	384-400,1.124; 151-157,1.056; 192-203,1.102; 501-509,1.105; 226-233,1.15; 63-69,1.064; 597-620,1.201; 478-484,1.077; 36-47,1.199; 170-183,1.099; 512-519,1.074; 491-497,1.068; 8-23,1.223; 240-254,1.178; 338-363,1.159; 523-533,1.076; 376-382,1.07; 444-469,1.135; 624-630,1.038; 295-336,1.235; 577-584,1.097; 259-268,1.096; 52-59,1.073; 108-147,1.127; 412-	PKC_PHOSPHO_SITE 496-498; CK2_PHOSPHO_SITE 121-124; MYRISTYL 254-259; CK2_PHOSPHO_SITE 496-499; CK2_PHOSPHO_SITE 367-370; ASN_GLYCOSYLATION 63-66; CK2_PHOSPHO_SITE 483-486; PKC_PHOSPHO_SITE 518-520; PKC_PHOSPHO_SITE 402-404; PKC_PHOSPHO_SITE 471-473; CK2_PHOSPHO_SITE 23-26; MYRISTYL 77-82; MYRISTYL 628-633; AMIDATION 159-162; PKC_PHOSPHO_SITE 159-161; TYR_PHOSPHO_SITE 57-64; RGD 468-470; TYR_PHOSPHO_SITE 380-388; MYRISTYL 588-593; ASN_GLYCOSYLATION 548-551;	SP_060568_PLO3_HUMAN 516-596;

				419,1.107; 559-575,1.156;	PKC PHOSPHO_SITE 633-635; MYRISTYL 167-172; CK2_PHOSPHO_SITE 487-490; CK2_PHOSPHO_SITE 485-488; CK2_PHOSPHO_SITE 433-436; PKC_PHOSPHO_SITE 25-27; MYRISTYL 278-283; PKC_PHOSPHO_SITE 65-67; CK2_PHOSPHO_SITE 519-522;	
DEX0450 018.aa.2	Y	0 - 01- 682;		295-336,1.235; 8-23,1.223; 523-533,1.076; 226- 233,1.15; 512-519,1.074; 491-497,1.068; 638- 645,1.074; 478-484,1.077; 338-363,1.159; 376- 382,1.07; 259-268,1.096; 649-666,1.151; 612- 618,1.086; 501-509,1.105; 52-59,1.073; 151-157,1.056; 412-419,1.107; 36-47,1.199; 384-400,1.124; 192- 203,1.102; 444-469,1.135; 577-584,1.097; 559- 575,1.156; 170-183,1.099; 63-69,1.064; 240-254,1.178; 108-147,1.127;	ASN GLYCOSYLATION 624-627; MYRISTYL 278-283; CK2_PHOSPHO_SITE 519-522; MYRISTYL 254-259; CK2_PHOSPHO_SITE 487-490; MYRISTYL 625-630; RGD 468-470; CK2_PHOSPHO_SITE 433-436; CK2_PHOSPHO_SITE 367-370; PKC_PHOSPHO_SITE 25-27; CK2_PHOSPHO_SITE 485-488; ASN GLYCOSYLATION 548-551; ASN GLYCOSYLATION 63-66; PKC_PHOSPHO_SITE 471-473; PKC_PHOSPHO_SITE 518-520; PKC_PHOSPHO_SITE 65-67; TYR_PHOSPHO_SITE 57-64; CK2_PHOSPHO_SITE 121-124; CK2_PHOSPHO_SITE 23-26; MYRISTYL 77-82; AMIDATION 159-162; CK2_PHOSPHO_SITE 483-486; MYRISTYL 632-637; PKC_PHOSPHO_SITE 496-498; PKC_PHOSPHO_SITE 159-161; TYR_PHOSPHO_SITE 380-388; MYRISTYL 167-172; MYRISTYL 588-593; CK2_PHOSPHO_SITE 496-499; PKC_PHOSPHO_SITE 402-404;	sp_060568_PLO3_HUMAN 516-612;
DEX0450 018.aa.3	Y	0 - 01- 654;		412-419,1.107; 611- 617,1.107; 108-147,1.127; 170-183,1.099; 444- 469,1.135; 338-363,1.159; 192-203,1.102; 63-69,1.064;	TYR_PHOSPHO_SITE 57-64; PKC_PHOSPHO_SITE 402-404; PKC_PHOSPHO_SITE 518-520; CK2_PHOSPHO_SITE 485-488; PKC_PHOSPHO_SITE 496-498;	sp_060568_PLO3_HUMAN 516-596;

			501-509, 1.105; 226-233, 1.15; 523-533, 1.076; 240-254, 1.178; 478-484, 1.077; 512-519, 1.074; 151-157, 1.056; 8-23, 1.223; 376-382, 1.07; 295-336, 1.235; 491-497, 1.068; 36-47, 1.199; 559-575, 1.156; 52-59, 1.073; 577-584, 1.097; 384-400, 1.124; 259-268, 1.096;	TYR_PHOSPHO_SITE 380-388; CK2_PHOSPHO_SITE 483-486; RGD 468-470; CK2_PHOSPHO_SITE 487-490; PKC_PHOSPHO_SITE 471-473; ASN_GLYCOSYLATION 548-551; AMIDATION 159-162; CK2_PHOSPHO_SITE 617-620; CK2_PHOSPHO_SITE 519-522; PKC_PHOSPHO_SITE 648-650; CK2_PHOSPHO_SITE 23-26; CK2_PHOSPHO_SITE 496-499; CK2_PHOSPHO_SITE 121-124; PKC_PHOSPHO_SITE 25-27; MYRISTYL 167-172; MYRISTYL 612-617; CK2_PHOSPHO_SITE 433-436; MYRISTYL 647-652; MYRISTYL 77-82; ASN_GLYCOSYLATION 63-66; MYRISTYL 599-604; CK2_PHOSPHO_SITE 367-370; MYRISTYL 254-259; PKC_PHOSPHO_SITE 159-161; MYRISTYL 278-283; MYRISTYL 588-593; PKC PHOSPHO SITE 65-67;	
DEX0450-018.orf.3	Y	0 - ol-669;		PKC_PHOSPHO_SITE 533-535; MYRISTYL 603-608; CK2_PHOSPHO_SITE 632-635; ASN_GLYCOSYLATION 563-566; PKC_PHOSPHO_SITE 511-513; TYR_PHOSPHO_SITE 395-403; MYRISTYL 92-97; AMIDATION 174-177; CK2_PHOSPHO_SITE 500-503; CK2_PHOSPHO_SITE 382-385; PKC_PHOSPHO_SITE 417-419; MYRISTYL 613-618; RGD 483-485; ASN_GLYCOSYLATION 78-81; TYR_PHOSPHO_SITE 72-79; CK2_PHOSPHO_SITE 448-451; CK2_PHOSPHO_SITE 38-41; MYRISTYL 182-187; MYRISTYL 614-619; PKC_PHOSPHO_SITE 174-176; CK2 PHOSPHO SITE 498-501;	SP_060568_PLO3_HUMAN 531-611;

DEX0450- 018.aa.4	N	0 - 01- 411;	279-293,1.123; 140- 150,1.076; 364-375,1.157; 403-408,1.144; 129- 136,1.074; 152-159,1.102; 336-343,1.068; 347- 355,1.103; 167-172,1.063; 79-92,1.068; 178-184,1.106; 295-306,1.12; 250- 257,1.097; 116-126,1.105; 203-210,1.1; 66-72,1.077; 309-316,1.08; 43-57,1.135; 4-10,1.103; 232-248,1.156; 380-394,1.095; 322- 330,1.129; 96-111,1.09; 26- 33,1.097;	ASN_GLYCOSYLATION 613-616; CK2_PHOSPHO_SITE 136-139; MYRISTYL 627-632; PKC_PHOSPHO_SITE 80-82; MYRISTYL 269-274; PKC_PHOSPHO_SITE 40-42; PKC_PHOSPHO_SITE 486-488; MYRISTYL 293-298; CK2_PHOSPHO_SITE 502-505; CK2_PHOSPHO_SITE 534-537; PKC_PHOSPHO_SITE 663-665; CK2_PHOSPHO_SITE 511-514; MYRISTYL 662-667; CK2_PHOSPHO_SITE 17-20; MYRISTYL 199-204; CK2_PHOSPHO_SITE 18-21; PKC_PHOSPHO_SITE 336-338; MYRISTYL 41-46; PKC_PHOSPHO_SITE 84-86; CAMP_PHOSPHO_SITE 15-18; CK2_PHOSPHO_SITE 75-78; MYRISTYL 394-399; MYRISTYL 37-42; MYRISTYL 275-280; CK2_PHOSPHO_SITE 84-87; RGD 56-58; CK2_PHOSPHO_SITE 175-178; PKC_PHOSPHO_SITE 135-137; PKC_PHOSPHO_SITE 175-177; CK2_PHOSPHO_SITE 407-410; PKC_PHOSPHO_SITE 187-189; MYRISTYL 35-40; CK2_PHOSPHO_SITE 136-139; MYRISTYL 92-97; PKC_PHOSPHO_SITE 17- 19; CK2_PHOSPHO_SITE 73-76; AMIDATION 13-16; MYRISTYL 166-171; CK2_PHOSPHO_SITE 71-74; PKC_PHOSPHO_SITE 375-377; ASN_GLYCOSYLATION 221-224; PKC_PHOSPHO_SITE 59-61; MYRISTYL 261-266; CK2_PHOSPHO_SITE 19-22; PKC_PHOSPHO_SITE 31-33; MYRISTYL 105-110; PKC_PHOSPHO_SITE 180-182; MYRISTYL 10-15; PKC_PHOSPHO_SITE 3-	sp_060568_PLO3_HUMAN 133-155; 20G-FeII_Oxy 320-411; LYS_HYDROXYLASE 339- 346; P4Hc 237-410; sp_060568_PLO3_HUMAN 212-411;
DEX0450- 018.orf. 4	N	0 - 01- 255;	153-160,1.08; 123- 137,1.123; 180-187,1.068; 94-101,1.097; 76-92,1.156; 22-28,1.106; 191-199,1.103;	CK2_PHOSPHO_SITE 19-22; PKC_PHOSPHO_SITE 31-33; MYRISTYL 105-110; PKC_PHOSPHO_SITE 180-182; MYRISTYL 10-15; PKC_PHOSPHO_SITE 3-	20G-FeII_Oxy 164-255; P4Hc 81-254; LYS_HYDROXYLASE 183- 190;

				139-150,1.1.12; 47-54,1.1.1; 208-219,1.1.157; 247- 252,1.1.144; 166-174,1.1.129; 11-16,1.0.63; 224-238,1.0.95;		5; MYRISTYL 119-124; ASN GLYCOSYLATION 65-68; MYRISTYL 43-48; MYRISTYL 238-243; CK2_PHOSPHO_SITE 251-254; PKC_PHOSPHO_SITE 19-21; PKC PHOSPHO_SITE 219-221;	SP_060568_PLO3_HUMAN 56-255;
DEX0450_019.aa.1	N	0 - ol-312;	282-291,1.1.119; 249- 258,1.0.43; 37-55,1.1.146; 83- 104,1.1.142; 58-79,1.1.128; 225-240,1.1.194; 110- 119,1.1.102; 206-213,1.1.1; 145-152,1.1.111; 261- 274,1.2.17; 194-200,1.0.74;		AMIDATION 259-262; MYRISTYL 79-84; MYRISTYL 11-16; AMIDATION 191-194; MYRISTYL 159-164; MYRISTYL 243-248; ASN GLYCOSYLATION 211-214; MYRISTYL 165-170; PKC_PHOSPHO_SITE 274-276; MYRISTYL 59-64; ASN GLYCOSYLATION 303-306; MYRISTYL 173-178; MYRISTYL 47-52; PKC_PHOSPHO_SITE 200-202; CK2_PHOSPHO_SITE 184-187; MYRISTYL 167-172; MYRISTYL 128-133; TYR_PHOSPHO SITE 69-76; MYRISTYL 134-139; MYRISTYL 130-135; MYRISTYL 207-212; MYRISTYL 154-159; CK2 PHOSPHO SITE 200-203;	PROTEASOME 44-59; PROTEASOME 201-212; PROTEASOME_B 40-87; PROTEASOME 165-176; proteasome 33-215; PROTEASOME_PROTEASE 35- 200; PROTEASOME 176- 187;	
DEX0450_019.orf.1	N	0 - ol-299;	35-41,1.0.9; 135-156,1.1.128; 160-181,1.1.142; 114- 132,1.1.146; 12-31,1.1.157; 271-277,1.0.74; 222- 229,1.1.111; 283-290,1.1.1; 57- 64,1.1.102; 187-196,1.1.102;		CK2_PHOSPHO_SITE 261-264; AMIDATION 65-68; PKC_PHOSPHO_SITE 277-279; MYRISTYL 244-249; MYRISTYL 242-247; MYRISTYL 156-161; AMIDATION 268-271; MYRISTYL 43-48; MYRISTYL 40-45; MYRISTYL 250-255; MYRISTYL 211-216; PKC_PHOSPHO_SITE 65-67; ASN GLYCOSYLATION 288-291; TYR_PHOSPHO_SITE 146-153; MYRISTYL 136-141; MYRISTYL 124-129; TYR_PHOSPHO_SITE 67-74; PKC_PHOSPHO_SITE 4-6; MYRISTYL 231- 236; PKC_PHOSPHO_SITE 50-52; CK2_PHOSPHO_SITE 277-280; MYRISTYL 236-241; MYRISTYL 207-212; MYRISTYL 205-210; MYRISTYL 88-93;	PROTEASOME_PROTEASE 112-277; PROTEASOME 121-136; PROTEASOME_B 117-164; PROTEASOME 242-253; proteasome 110-292; PROTEASOME 278-289; PROTEASOME 253-264;	

				PKC_PHOSPHO_SITE 77-79; MYRISTYL 284-289;	
DEX0450-019.aa.2	N	0 - 01-274;	206-212,1.1; 110-119,1.102; 58-79,1.128; 194-200,1.074; 83-104,1.142; 37-55,1.146; 145-152,1.111; 253-259,1.097;	MYRISTYL 154-159; PKC_PHOSPHO_SITE 219-221; MYRISTYL 11-16; AMIDATION 191-194; MYRISTYL 165-170; MYRISTYL 159-164; PKC_PHOSPHO_SITE 248-250; MYRISTYL 134-139; CAMP_PHOSPHO_SITE 249-252; MYRISTYL 173-178; MYRISTYL 47-52; CK2_PHOSPHO_SITE 200-203; MYRISTYL 128-133; MYRISTYL 79-84; MYRISTYL 207-212; MYRISTYL 59-64; MYRISTYL 254-259; MYRISTYL 167-172; TYR_PHOSPHO_SITE 69-76; CK2_PHOSPHO_SITE 184-187; PKC_PHOSPHO_SITE 200-202; MYRISTYL 130-135;	PROTEASOME 44-59; PROTEASOME 165-176; PROTEASOME_PROTEASE 35-200; PROTEASOME 176-187; PROTEASOME 201-212; PROTEASOME_B 40-87; proteasome 33-215;
DEX0450-019.crf.2	N	0 - 01-294;	222-229,1.111; 114-132,1.146; 283-289,1.1; 160-181,1.142; 135-156,1.128; 271-277,1.074; 12-31,1.157; 187-196,1.102; 35-41,1.09; 57-64,1.102;	CK2_PHOSPHO_SITE 261-264; AMIDATION 268-271; TYR_PHOSPHO_SITE 146-153; MYRISTYL 284-289; MYRISTYL 231-236; PKC_PHOSPHO_SITE 77-79; PKC_PHOSPHO_SITE 65-67; MYRISTYL 136-141; MYRISTYL 43-48; MYRISTYL 211-216; PKC_PHOSPHO_SITE 4-6; AMIDATION 65-68; MYRISTYL 250-255; MYRISTYL 88-93; MYRISTYL 236-241; MYRISTYL 40-45; PKC_PHOSPHO_SITE 277-279; MYRISTYL 124-129; TYR_PHOSPHO_SITE 67-74; MYRISTYL 207-212; MYRISTYL 244-249; MYRISTYL 156-161; PKC_PHOSPHO_SITE 50-52; MYRISTYL 242-247; MYRISTYL 205-210; CK2_PHOSPHO_SITE 277-280;	proteasome 110-292; PROTEASOME 242-253; PROTEASOME 253-264; PROTEASOME 278-289; PROTEASOME 121-136; PROTEASOME_PROTEASE 112-277; PROTEASOME_B 117-164;
DEX0450-019.aa.3	N	0 - 01-237;	58-79,1.128; 222-233,1.175; 37-55,1.146; 83-104,1.142; 194-200,1.074; 206-213,1.112; 145-152,1.111;	MYRISTYL 59-64; MYRISTYL 130-135; MYRISTYL 167-172; MYRISTYL 11-16; CK2_PHOSPHO_SITE 200-203; MYRISTYL 154-159; PKC_PHOSPHO_SITE 200-202;	proteasome 33-215; PROTEASOME 201-212; PROTEASOME 176-187; PROTEASOME_B 40-87;

			110-119, 1.102;	MYRISTYL 159-164; MYRISTYL 165-170; CK2_PHOSPHO_SITE 223-226; MYRISTYL 79-84; MYRISTYL 47-52; CK2_PHOSPHO_SITE 184-187; MYRISTYL 134-139; AMIDATION 191-194; MYRISTYL 128-133; MYRISTYL 173-178; TYR_PHOSPHO_SITE 69-76; MYRISTYL 207-212;	PROTEASOME 165-176; PROTEASOME_PROTEASE 35- 200; PROTEASOME 44-59;
DEX0450- 019.orf. 3	N	0 - ol- 297;		TYR_PHOSPHO_SITE 67-74; MYRISTYL 236-241; MYRISTYL 250-255; TYR_PHOSPHO_SITE 146-153; MYRISTYL 207-212; CK2_PHOSPHO_SITE 277-280; AMIDATION 268-271; MYRISTYL 211-216; PKC_PHOSPHO_SITE 50-52; AMIDATION 65-68; MYRISTYL 156-161; MYRISTYL 40-45; PKC_PHOSPHO_SITE 277-279; PKC_PHOSPHO_SITE 4-6; MYRISTYL 88- 93; MYRISTYL 284-289; PKC_PHOSPHO_SITE 77-79; MYRISTYL 231-236; MYRISTYL 244-249; MYRISTYL 124-129; MYRISTYL 136-141; PKC_PHOSPHO_SITE 65-67; MYRISTYL 205-210; MYRISTYL 43-48; CK2_PHOSPHO_SITE 261-264; MYRISTYL 242-247;	PROTEASOME_PROTEASE 112-277; Proteasome 110-292; PROTEASOME 253-264; PROTEASOME 121-136; PROTEASOME 242-253; PROTEASOME 278-289; PROTEASOME_B 117-164;
DEX0450- 020.aa.1	N	0 - ol- 260;	198-213, 1.076; 128- 145, 1.093; 53-71, 1.181; 238-254, 1.196; 151- 161, 1.056; 40-50, 1.103; 223-233, 1.092; 97- 104, 1.099; 163-174, 1.09; 5- 16, 1.088; 20-38, 1.144;	PKC_PHOSPHO_SITE 75-77; CK2_PHOSPHO_SITE 16-19; CK2_PHOSPHO_SITE 256-259; LEUCINE_ZIPPER 55-76; PKC_PHOSPHO_SITE 161-163; MYRISTYL 157-162; CK2_PHOSPHO_SITE 51-54; MYRISTYL 160-165; LEUCINE_ZIPPER 48- 69; MYRISTYL 85-90; MYRISTYL 119- 124;	
DEX0450- 020.orf.	N	0 - ol- 249;	29-39, 1.103; 117-134, 1.093; 4-27, 1.144; 212-222, 1.092;	MYRISTYL 146-151; CK2_PHOSPHO_SITE 40-43; PKC PHOSPHO_SITE 150-152;	

1				152-163,1.09; 86-93,1.099; 140-150,1.056; 42-60,1.181; 187-202,1.076; 227- 243,1.196;	MYRISTYL 108-113; MYRISTYL 74-79; LEUCINE_ZIPPER 37-58; PKC_PHOSPHO_SITE 64-66; LEUCINE_ZIPPER 44-65; MYRISTYL 149- 154; CK2_PHOSPHO_SITE 245-248;	
DEX0450- 020.aa.2	Y	0 - ol- 132;		4-12,1.075; 41-71,1.185; 15-27,1.203; 31-37,1.04; 75-119,1.163;	MYRISTYL 31-36; CK2_PHOSPHO_SITE 101-104; PKC_PHOSPHO_SITE 117-119; ASN_GLYCOSYLATION 122-125; MYRISTYL 71-76;	
DEX0450- 020.orf. 2	N	0 - ol- 225;			MYRISTYL 108-113; TYR_PHOSPHO_SITE 15-23; AMIDATION 13-16; CK2_PHOSPHO_SITE 4-7; PKC_PHOSPHO_SITE 105-107; MYRISTYL 112-117; CK2_PHOSPHO_SITE 119-122; MYRISTYL 43-48; PKC_PHOSPHO_SITE 13- 15; PKC_PHOSPHO_SITE 23-25; CK2_PHOSPHO_SITE 91-94; MYRISTYL 44- 49; MYRISTYL 149-154; MYRISTYL 10- 15; CK2_PHOSPHO_SITE 69-72; MYRISTYL 153-158;	
DEX0450- 020.orf. 3	N	0 - ol- 451;		145-150,1.066; 152- 159,1.121; 105-111,1.059; 325-335,1.245; 410- 419,1.079; 248-254,1.06; 4- 46,1.165; 261-272,1.059; 182-189,1.057; 390- 402,1.179; 192-201,1.027; 74-93,1.186; 423-429,1.048; 317-322,1.064; 307- 314,1.056; 120-137,1.13; 203-211,1.047; 294- 300,1.081; 162-168,1.08; 213-219,1.076; 229- 235,1.094; 377-385,1.072; 344-349,1.045;	MYRISTYL 239-244; PKC_PHOSPHO_SITE 135-137; CK2_PHOSPHO_SITE 201-204; LEUCINE_ZIPPER 401-422; PKC_PHOSPHO_SITE 256-258; CK2_PHOSPHO_SITE 220-223; PKC_PHOSPHO_SITE 224-226; MYRISTYL 69-74; MYRISTYL 188-193; PKC_PHOSPHO_SITE 38-40; MYRISTYL 296-301; MYRISTYL 178-183; PKC_PHOSPHO_SITE 277-279; CK2_PHOSPHO_SITE 310-313; PKC_PHOSPHO_SITE 282-284; MYRISTYL 295-300; MYRISTYL 175-180; LEUCINE_ZIPPER 408-429; CK2_PHOSPHO_SITE 350-353; MYRISTYL 215-220; MYRISTYL 290-295; MYRISTYL	PRICHEXTENSIN 150-171; PRICHEXTENSIN 47-59; GLN_RICH 383-421; SER_RICH 192-310; PRICHEXTENSIN 311-323;

163

DEX0450_021.aa.1	N	0 - 01-1193;	<p>453-472,1.23; 1066-1072,1.099; 819-830,1.099; 977-999,1.127; 1088-1095,1.087; 720-735,1.111; 287-301,1.237; 895-917,1.103; 218-229,1.127; 572-600,1.117; 836-846,1.212; 235-253,1.178; 1180-1190,1.121; 965-970,1.052; 367-380,1.119; 59-65,1.053; 541-565,1.112; 435-450,1.182; 304-313,1.107; 675-690,1.192; 1097-1106,1.185; 755-764,1.088; 5-14,1.075; 322-330,1.145; 951-961,1.084; 18-30,1.082; 417-423,1.079; 42-47,1.063; 1109-1114,1.05; 269-280,1.136; 607-619,1.136; 190-214,1.152; 1130-1135,1.064; 176-182,1.048; 332-352,1.217; 400-407,1.062; 880-893,1.178; 778-810,1.167; 90-106,1.105; 767-775,1.058; 624-635,1.134; 486-500,1.153; 1028-1033,1.072; 711-718,1.065; 510-515,1.032; 386-394,1.121; 861-871,1.159;</p>	<p>31-36; MYRISTYL 287-292; CK2_PHOSPHO_SITE 273-276; CK2_PHOSPHO_SITE 109-112; MYRISTYL 65-70; MYRISTYL 255-260; LEUCINE ZIPPER 394-415;</p> <p>CAMP_PHOSPHO_SITE 990-993; CAMP_PHOSPHO_SITE 1165-1168; PKC_PHOSPHO_SITE 427-429; PKC_PHOSPHO_SITE 959-961; CK2_PHOSPHO_SITE 959-962; ASN_GLYCOSYLATION 1126-1129; PKC_PHOSPHO_SITE 404-406; MYRISTYL 14-19; PKC_PHOSPHO_SITE 77-79; CK2_PHOSPHO_SITE 313-316; PKC_PHOSPHO_SITE 167-169; MYRISTYL 569-574; PKC_PHOSPHO_SITE 149-151; CK2_PHOSPHO_SITE 351-354; CK2_PHOSPHO_SITE 118-121; MYRISTYL 552-557; CK2_PHOSPHO_SITE 825-828; PKC_PHOSPHO_SITE 729-731; CK2_PHOSPHO_SITE 526-529; CK2_PHOSPHO_SITE 350-353; PKC_PHOSPHO_SITE 26-28; MYRISTYL 853-858; PKC_PHOSPHO_SITE 704-706; CK2_PHOSPHO_SITE 209-212; PKC_PHOSPHO_SITE 231-233; CK2_PHOSPHO_SITE 427-430; CK2_PHOSPHO_SITE 1054-1057; ASN_GLYCOSYLATION 722-725; PKC_PHOSPHO_SITE 645-647; CK2_PHOSPHO_SITE 993-996; CK2_PHOSPHO_SITE 83-86; ASN_GLYCOSYLATION 1177-1180; CK2_PHOSPHO_SITE 187-190; CK2_PHOSPHO_SITE 194-197; ASN_GLYCOSYLATION 863-866; MYRISTYL 847-852; PKC_PHOSPHO_SITE 1162-1164;</p>	<p>VINCULIN 588-601; VINCULIN 572-582; FH2 636-1077; PRO_RICH 561-636; RNASE_PANCREATIC 680-686; FH2 636-1077; PRICHEXTENSIN 573-594; PRICHEXTENSIN 598-614;</p>
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DEX0450_022.aa.1	N	0 - 01-650;	80-87, 1.064; 202-208, 1.098; 452-473, 1.096; 48-54, 1.088; 163-172, 1.164; 4-12, 1.085; 602-614, 1.141; 505-537, 1.219; 216-226, 1.094; 479-503, 1.208; 108-113, 1.065; 425-449, 1.141; 244-254, 1.104; 156-161, 1.052; 542-554, 1.175; 380-396, 1.161; 626-637, 1.111; 41-46, 1.047; 570-576, 1.065; 89-102, 1.126; 292-308, 1.145; 231-237, 1.042; 264-286, 1.134; 125-140, 1.114; 334-348, 1.136;	CK2_PHOSPHO_SITE 1175-1178; CK2_PHOSPHO_SITE 175-178; CK2_PHOSPHO_SITE 431-434; PKC_PHOSPHO_SITE 83-85; MYRISTYL 29-34; PKC_PHOSPHO_SITE 198-200; MYRISTYL 329-334; TYR_PHOSPHO_SITE 667-673; CK2_PHOSPHO_SITE 66-69; TYR_PHOSPHO_SITE 411-418; CK2_PHOSPHO_SITE 48-51; PKC_PHOSPHO_SITE 1127-1129; CK2_PHOSPHO_SITE 302-305; CK2_PHOSPHO_SITE 1179-1182; PKC_PHOSPHO_SITE 1146-1148; MYRISTYL 1060-1065; PKC_PHOSPHO_SITE 480-482; CAMP_PHOSPHO_SITE 1079-1082; PKC_PHOSPHO_SITE 1096-1098;	
			PKC_PHOSPHO_SITE 419-421; MYRISTYL 624-629; MYRISTYL 176-181; PKC_PHOSPHO_SITE 358-360; PKC_PHOSPHO_SITE 539-541; CK2_PHOSPHO_SITE 617-620; PKC_PHOSPHO_SITE 375-377; MYRISTYL 369-374; CK2_PHOSPHO_SITE 39-42; MYRISTYL 398-403; PKC_PHOSPHO_SITE 119-121; CK2_PHOSPHO_SITE 180-183; ASN_GLYCOSYLATION 98-101; CK2_PHOSPHO_SITE 307-310; PKC_PHOSPHO_SITE 581-583; ASN_GLYCOSYLATION 218-221; MYRISTYL 233-238; MYRISTYL 236-241; CK2_PHOSPHO_SITE 558-561; MYRISTYL 363-368; ASN_GLYCOSYLATION 240-243; MYRISTYL 224-229; CK2_PHOSPHO_SITE 138-141; ASN_GLYCOSYLATION 161-164; ASN_GLYCOSYLATION 198-201; CK2_PHOSPHO_SITE 2-5; PKC_PHOSPHO_SITE 47-49;	PRICHEXTENS 456-481; PRICHEXTENS 334-346; SP_Q9H271_Q9H271_HUMAN 190-334; PRO_RICH 334-557; NOP 186-334; PRICHEXTENS 425-442;	

					TYR_PHOSPHO_SITE 559-565; PKC_PHOSPHO_SITE 617-619; MYRISTYL 20-25; MYRISTYL 497-502; MYRISTYL 613-618; CK2_PHOSPHO_SITE 22-25; PKC PHOSPHO SITE 138-140;		
DEX0450- 022.orf. 1	N	0 - ol- 369;	100-113,1.126; 345- 359,1.136; 59-65,1.088; 303-319,1.145; 15-23,1.085; 174-183,1.164; 275- 297,1.134; 167-172,1.052; 227-237,1.094; 91-98,1.064; 136-151,1.114; 119- 124,1.065; 255-265,1.104; 242-248,1.042; 52-57,1.047; 213-219,1.098;	ASN_GLYCOSYLATION 172-175; MYRISTYL 9-14; PKC_PHOSPHO_SITE 149-151; MYRISTYL 235-240; ASN_GLYCOSYLATION 251-254; CK2_PHOSPHO_SITE 33-36; MYRISTYL 244-249; CK2_PHOSPHO_SITE 318-321; CK2_PHOSPHO_SITE 13-16; ASN_GLYCOSYLATION 209-212; CK2_PHOSPHO_SITE 50-53; MYRISTYL 187-192; MYRISTYL 11-16; ASN_GLYCOSYLATION 229-232; AMIDATION 366-369; MYRISTYL 247-252; MYRISTYL 31-36; CK2_PHOSPHO_SITE 191-194; PKC PHOSPHO SITE 130-132; CK2_PHOSPHO SITE 149-152; ASN_GLYCOSYLATION 109-112; PKC PHOSPHO SITE 58-60;	sp_Q9H271_Q9H271_HUMAN 201-345; Nop 197-345;		
DEX0450- 023.aa.1	Y	0 - ol- 164;	27-32,1.031; 116-135,1.152; 54-59,1.094; 74-89,1.127; 101-114,1.102; 39-48,1.106; 150-159,1.138; 6-23,1.08;	PKC_PHOSPHO_SITE 124-126; CK2_PHOSPHO_SITE 67-70; CAMP_PHOSPHO_SITE 138-141; MYRISTYL 15-20; MYRISTYL 105-110; MYRISTYL 54-59; CK2_PHOSPHO_SITE 91-94; MYRISTYL 32-37; CK2_PHOSPHO_SITE 38- 41; AMIDATION 136-139; PKC PHOSPHO SITE 24-26; CK2_PHOSPHO SITE 96-99; PKC PHOSPHO SITE 96-98;	ER_TARGET 161-164; THIOREDOXIN 73-81; THIOREDOXIN 74-92; THIOREDOXIN_2 55-158; THIOREDOXIN 81-90; THIOREDOXIN 124-135; thioered 53-161;		
DEX0450- 023.aa.2	N	0 - il- 31;	17-28,1.096; 5-13,1.067;	TYR_PHOSPHO_SITE 13-19; PKC_PHOSPHO_SITE 11-13; CK2_PHOSPHO_SITE 24-27;			
DEX0450- 023.orf.	N	0 - ol- 110;	4-11,1.144; 80-99,1.195; 35-63,1.145;	ASN_GLYCOSYLATION 31-34; CK2 PHOSPHO SITE 13-16;			

2					ASN GLYCOSYLATION 100-103;	
DEX0450_023.aa.3	N	1 - i1-20;tm21-38;o39-39;	19-36,1.212;			
DEX0450_023.orf.3	N	0 - o1-110;	80-99,1.195; 4-11,1.144; 35-63,1.145;		ASN GLYCOSYLATION 100-103; CK2_PHOSPHO_SITE 13-16; ASN GLYCOSYLATION 31-34;	
DEX0450_024.aa.1	N	0 - o1-140;	35-42,1.129; 111-137,1.283; 65-89,1.119; 4-13,1.181; 26-31,1.071; 94-104,1.167;		AMIDATION 2-5; PKC_PHOSPHO_SITE 52-54; CK2_PHOSPHO_SITE 52-55; PKC_PHOSPHO_SITE 13-15; PKC_PHOSPHO_SITE 57-59;	Flavodoxin_2 4-140;
DEX0450_025.aa.1	N	0 - o1-73;	19-28,1.168; 62-70,1.085;		CK2_PHOSPHO_SITE 41-44; MYRISTYL 28-33;	SP_O77641_CATK_MACFA 7-71; PAPAIN 35-41; THIOL_PROTEASE ASN 35-54; PAPAIN 20-30; THIOL_PROTEASE_HIS 18-28;
DEX0450_025.orf.1	N	0 - o1-72;	18-27,1.168; 60-69,1.085;		PKC_PHOSPHO_SITE 1-3; MYRISTYL 27-32; CK2_PHOSPHO_SITE 40-43;	PAPAIN 34-40; PAPAIN 19-29; SP_O77641_CATK_MACFA 4-70; THIOL_PROTEASE_HIS 17-27; THIOL_PROTEASE ASN 34-53;
DEX0450_026.aa.1	Y	7 - o1-19;tm20-42;i43-54;tm55-77;o78-80;tm81-103;i104-119;tm120-142;o143-	4-253,1.334; 263-270,1.114; 282-318,1.14;		MYRISTYL 273-278; PKC_PHOSPHO_SITE 294-296; PKC_PHOSPHO_SITE 170-172; PKC_PHOSPHO_SITE 167-169; PKC_PHOSPHO_SITE 10-12; MYRISTYL 232-237; LEUCINE_ZIPPER 124-145; MYRISTYL 7-12;	LEU RICH 56-229; PHE_RICH 16-168;

		151;tm152 - 171;i172- 177;tm178 - 200;o201- 223;tm224 - 246;i247- 321;				
DEX0450- 026.orf. 1	Y	8 - i1- 1;tm2- 19;o20- 23;tm24- 46;i47- 84;tm85- 107;o108- 116;tm117 - 139;i140- 145;tm146 - 168;o169- 200;tm201 - 223;i224- 229;tm230 - 252;o253- 295;tm296 - 318;i319- 320;	4-194,1.278; 275-317,1.166; 197-262,1.381;	CAMP_PHOSPHO_SITE 260-263; PKC_PHOSPHO_SITE 81-83; MYRISTYL 61- 66; MYRISTYL 40-45; PKC_PHOSPHO_SITE 258-260;	LEU_RICH 2-175; C_TYPE_LLECTIN_1 102- 128; CYS_RICH 218-246;	
DEX0450- 026.orf. 2	Y	8 - i1- 1;tm2- 19;o20-	197-262,1.381; 275- 317,1.166; 4-194,1.278;	PKC_PHOSPHO_SITE 258-260; CAMP_PHOSPHO_SITE 260-263; PKC PHOSPHO SITE 81-83; MYRISTYL 61-	LEU_RICH 2-175; CYS_RICH 218-246; C TYPE LLECTIN 1 102-	

		23;tm24-46;i47-84;tm85-107;o108-116;tm117-139;i140-145;tm146-168;o169-200;tm201-223;i224-229;tm230-252;o253-295;tm296-318;i319-320;		66; MYRISTYL 40-45;	128;
DEX0450_027.aa.1	N	0 - 01-684;	158-165,1.097; 291-299,1.087; 21-28,1.156; 120-132,1.207; 59-93,1.114; 141-156,1.088; 220-233,1.091; 611-619,1.092; 211-216,1.072; 175-184,1.105; 13-19,1.104; 631-638,1.103; 41-56,1.122; 646-652,1.094; 30-39,1.108; 277-289,1.132; 461-466,1.074; 507-514,1.12; 346-352,1.057; 111-117,1.079; 493-499,1.072; 301-313,1.124; 547-554,1.112; 534-542,1.186; 396-402,1.035; 429-450,1.14; 250-256,1.067;	AMIDATION 403-406; TYR_PHOSPHO_SITE 238-245; MYRISTYL 106-111; PKC_PHOSPHO_SITE 677-679; ASN_GLYCOSYLATION 458-461; MYRISTYL 289-294; MYRISTYL 329-334; CK2_PHOSPHO_SITE 625-628; LEUCINE ZIPPER 68-89; ASN_GLYCOSYLATION 367-370; AMIDATION 451-454; AMIDATION 677-680; CK2_PHOSPHO_SITE 45-48; PKC_PHOSPHO_SITE 441-443; AMIDATION 639-642; CAMP_PHOSPHO_SITE 480-483; CK2_PHOSPHO_SITE 7-10; CAMP_PHOSPHO_SITE 405-408; PKC_PHOSPHO_SITE 7-9; PKC_PHOSPHO_SITE 111-113; PKC PHOSPHO_SITE 478-480;	TPR_REPEAT_2 242-275; TPR_REGION_1 62-135; TPR_REGION_2 202-355; TPR_REPEAT_3 282-315; TPR_REPEAT_4 322-355; TPR 102-135; GoLoco 594-616; GoLoco 628-650; TPR 62-95; GoLoco 628-650; TPR 142-188; TPR 62-95; TPR 282-315; TPR 322-355; TPR 242-275; GoLoco 489-511; TPR 142-188; TPR 202-235; TPR 102-135; TPR 282-315; TPR 322-355; SD 042393 RAPS CHICK

			598-607,1.155; 325-335,1.054; 578-585,1.147; 188-195,1.16; 566-573,1.067; 624-629,1.03; 266-274,1.136; 371-378,1.135;	PKC_PHOSPHO_SITE 501-503; PKC_PHOSPHO_SITE 460-462; PKC_PHOSPHO_SITE 363-365; ASN_GLYCOSYLATION 382-385; CK2_PHOSPHO_SITE 23-26; CK2_PHOSPHO_SITE 94-97; PKC_PHOSPHO_SITE 620-622; LEUCINE_ZIPPER 61-82; PKC_PHOSPHO_SITE 556-558; MYRISTYL 571-576; CK2_PHOSPHO_SITE 260-263; CK2_PHOSPHO_SITE 486-489; CK2_PHOSPHO_SITE 607-610; MYRISTYL 206-211; ASN_GLYCOSYLATION 188-191; CK2_PHOSPHO_SITE 390-393; MYRISTYL 376-381;	172-356; GoLoco 544-566; TPR 242-275; TPR_REPEAT_1 62-95; GoLoco 544-566; TPR 202-235; GoLoco 489-511;
DEX0450_028.aa.1	N	0 - 01-499;	247-262,1.118; 106-113,1.132; 195-204,1.181; 320-341,1.163; 476-485,1.094; 161-182,1.143; 224-245,1.198; 356-366,1.115; 374-402,1.129; 82-96,1.116; 404-420,1.07; 118-129,1.111; 265-271,1.084; 424-456,1.183; 273-308,1.192; 40-58,1.139; 21-38,1.098; 143-157,1.176; 458-474,1.063; 98-103,1.078; 348-353,1.032;	PKC_PHOSPHO_SITE 390-392; CK2_PHOSPHO_SITE 439-442; PKC_PHOSPHO_SITE 241-243; CK2_PHOSPHO_SITE 138-141; PKC_PHOSPHO_SITE 63-65; CK2_PHOSPHO_SITE 423-426; MYRISTYL 95-100; PKC_PHOSPHO_SITE 116-118; MYRISTYL 133-138; CK2_PHOSPHO_SITE 341-344; MYRISTYL 294-299; CAMP_PHOSPHO_SITE 331-334; PKC_PHOSPHO_SITE 420-422; PKC_PHOSPHO_SITE 157-159; ASN_GLYCOSYLATION 446-449; CK2_PHOSPHO_SITE 241-244; MYRISTYL 314-319; CK2_PHOSPHO_SITE 306-309; ASN_GLYCOSYLATION 79-82; MYRISTYL 459-464; MYRISTYL 134-139; CAMP_PHOSPHO_SITE 113-116; MYRISTYL 465-470;	AMINOLPTASE 308-326; AMINOLPTASE 168-185; AMINOLPTASE 131-151; AMINOLPTASE 350-366; Peptidase_M18 34-435; AMINOLPTASE 98-114;
DEX0450_028.orf.	N	0 - 01-407;	98-112,1.116; 289-324,1.192; 281-287,1.084;	MYRISTYL 150-155; CK2_PHOSPHO_SITE 322-325; MYRISTYL 149-154; MYRISTYL	AMINOLPTASE 114-130; Peptidase_M18 50-407;

1			263-278, 1.118; 211-220, 1.181; 372-382, 1.115; 37-54, 1.098; 122-129, 1.132; 336-357, 1.163; 364-369, 1.032; 177-198, 1.143; 56-74, 1.139; 134-145, 1.111; 390-404, 1.129; 159-173, 1.176; 240-261, 1.198; 114-119, 1.078;	1-6; PKC_PHOSPHO_SITE 257-259; CAMP_PHOSPHO_SITE 129-132; CK2_PHOSPHO_SITE 357-360; MYRISTYL 111-116; PKC_PHOSPHO_SITE 132-134; MYRISTYL 310-315; CAMP_PHOSPHO_SITE 347-350; MYRISTYL 14-19; PKC_PHOSPHO_SITE 173-175; PKC_PHOSPHO_SITE 79-81; CK2_PHOSPHO_SITE 154-157; ASN_GLYCOSYLATION 95-98; CK2_PHOSPHO_SITE 257-260; MYRISTYL 15-20; MYRISTYL 330-335;	AMINO1PTASE 184-201; AMINO1PTASE 324-342; AMINO1PTASE 366-382; AMINO1PTASE 147-167;
DEX0450-029.aa.1	N	0 - 01-31;	17-28, 1.086;	CK2_PHOSPHO_SITE 5-8;	
DEX0450-029.orf.1	N	1 - 01-14; tm15-34; 135-69;	49-58, 1.065; 5-35, 1.167; 39-47, 1.084; 61-66, 1.186;	CK2_PHOSPHO_SITE 11-14; PKC_PHOSPHO_SITE 61-63; MYRISTYL 31-36; MYRISTYL 1-6;	
DEX0450-030.aa.1	N	0 - 11-89;	31-37, 1.049; 52-63, 1.073; 4-12, 1.091; 40-50, 1.107;	MYRISTYL 14-19; MYRISTYL 18-23; PKC_PHOSPHO_SITE 64-66; MYRISTYL 8-13; PKC_PHOSPHO_SITE 40-42; PKC_PHOSPHO_SITE 68-70;	THR_RICH 46-87;
DEX0450-030.orf.1	N	0 - 01-86;	49-60, 1.073; 37-47, 1.107; 28-34, 1.049;	MYRISTYL 14-19; PKC_PHOSPHO_SITE 61-63; PKC_PHOSPHO_SITE 37-39; PKC_PHOSPHO_SITE 65-67; MYRISTYL 2-7;	THR_RICH 43-84;
DEX0450-031.aa.1	N	1 - 11-98; tm99-121; 0122-404;	191-199, 1.133; 18-23, 1.038; 161-167, 1.103; 256-277, 1.166; 130-138, 1.071; 288-305, 1.202; 95-114, 1.206; 236-243, 1.078; 362-401, 1.221; 44-50, 1.087; 27-38, 1.189; 148-155, 1.071; 201-211, 1.157; 117-125, 1.108; 324-332, 1.126; 342-348, 1.06; 4-12, 1.043;	PKC_PHOSPHO_SITE 354-356; MYRISTYL 88-93; PKC_PHOSPHO_SITE 58-60; PKC_PHOSPHO_SITE 330-332; PKC_PHOSPHO_SITE 337-339; CK2_PHOSPHO_SITE 211-214; CAMP_PHOSPHO_SITE 53-56; PKC_PHOSPHO_SITE 277-279; CK2_PHOSPHO_SITE 58-61; MYRISTYL 97-102; ASN_GLYCOSYLATION 306-309; AMIDATION 83-86; ASN_GLYCOSYLATION	THYROGLOBULIN_1 278-307; TY 279-325; thyroglobulin_1 263-321;

					320-323; PKC_PHOSPHO_SITE 322-324; AMIDATION 51-54; ASN_GLYCOSYLATION 180-183; TYR_PHOSPHO_SITE 281-288; ASN_GLYCOSYLATION 186-189; MYRISTYL 113-118; CK2_PHOSPHO_SITE 75-78;		
DEX0450_031.orf.1	N	0 - ol-371;	97-105,1.071; 329-368,1.221; 255-272,1.202; 223-244,1.166; 128-134,1.103; 62-81,1.206; 168-178,1.157; 84-92,1.108; 309-315,1.06; 4-18,1.126; 203-210,1.078; 291-299,1.126; 158-166,1.133; 115-122,1.071;		AMIDATION 19-22; ASN_GLYCOSYLATION 153-156; PKC_PHOSPHO_SITE 304-306; ASN_GLYCOSYLATION 147-150; TYR_PHOSPHO_SITE 248-255; MYRISTYL 80-85; ASN_GLYCOSYLATION 287-290; MYRISTYL 64-69; PKC_PHOSPHO_SITE 289-291; AMIDATION 50-53; CK2_PHOSPHO_SITE 178-181; CK2_PHOSPHO_SITE 42-45; PKC_PHOSPHO_SITE 297-299; PKC_PHOSPHO_SITE 25-27; PKC_PHOSPHO_SITE 244-246; MYRISTYL 19-24; PKC_PHOSPHO_SITE 321-323; CK2_PHOSPHO_SITE 25-28; MYRISTYL 55-60; ASN_GLYCOSYLATION 273-276;	TY 246-292; thyroglobulin_1 230-288; THYROGLOBULIN_1 245-274;	
DEX0450_031.aa.2	N	0 - ol-102;	56-63,1.078; 89-95,1.067; 21-31,1.157;		CK2_PHOSPHO_SITE 93-96; CK2_PHOSPHO_SITE 31-34; MYRISTYL 89-94; GLYCOSAMINOGLYCAN 88-91;		
DEX0450_031.orf.2	N	0 - il-102;	62-75,1.231; 85-93,1.058; 38-48,1.152; 7-36,1.126;		CAMP_PHOSPHO_SITE 4-7; CK2_PHOSPHO_SITE 46-49; MYRISTYL 55-60;		
DEX0450_032.aa.1	N	0 - ol-273;	13-20,1.106; 175-192,1.139; 120-136,1.128; 30-57,1.253; 142-149,1.138; 4-9,1.134; 234-266,1.176; 64-102,1.179; 194-213,1.141;		PKC_PHOSPHO_SITE 267-269; MYRISTYL 201-206; CK2_PHOSPHO_SITE 29-32; ASN_GLYCOSYLATION 164-167; CK2_PHOSPHO_SITE 193-196; MYRISTYL 74-79; CK2_PHOSPHO_SITE 43-46; MYRISTYL 94-99; PKC_PHOSPHO_SITE 166-168; MYRISTYL 121-126;	RRM 181-255; RRM 182-251; rrm 183-250;	
DEX0450_032.orf.1	N	0 - ol-227;	4-14,1.073; 77-90,1.156; 148-167,1.141; 129-146,1.139; 19-66,1.216; 96-		CK2_PHOSPHO_SITE 147-150; PKC_PHOSPHO_SITE 120-122; MYRISTYL 155-160; MYRISTYL 37-42;	RRM 135-209; RRM 136-205; rrm 137-204;	

			103, 1.138; 188-220, 1.176;	PKC_PHOSPHO_SITE 221-223; MYRISTYL 64-69; MYRISTYL 77-82; AMIDATION 16-19; ASN_GLYCOSYLATION 118-121; CAMP_PHOSPHO_SITE 18-21; CK2_PHOSPHO_SITE 6-9;	
DEX0450-032.aa.2	Y	0 - 01-452;	35-60, 1.152; 236-250, 1.111; 102-119, 1.139; 224-234, 1.126; 69-76, 1.138; 26-32, 1.049; 167-175, 1.08; 371-382, 1.074; 300-319, 1.121; 403-409, 1.05; 324-343, 1.153; 411-419, 1.055; 5-17, 1.091; 384-393, 1.073; 189-208, 1.13; 257-292, 1.18; 151-160, 1.165; 121-140, 1.141;	PKC_PHOSPHO_SITE 93-95; ASN_GLYCOSYLATION 91-94; CK2_PHOSPHO_SITE 442-445; MYRISTYL 44-49; CK2_PHOSPHO_SITE 120-123; PKC_PHOSPHO_SITE 162-164; PKC_PHOSPHO_SITE 9-11; PKC_PHOSPHO_SITE 61-63; MYRISTYL 60-65; MYRISTYL 128-133; MYRISTYL 251-256; CK2_PHOSPHO_SITE 353-356; MYRISTYL 433-438; RGD 438-440; TYR_PHOSPHO_SITE 262-270; MYRISTYL 161-166; CK2_PHOSPHO_SITE 20-23; PKC_PHOSPHO_SITE 20-22; MYRISTYL 153-158; PKC_PHOSPHO_SITE 429-431; CAMP_PHOSPHO_SITE 62-65; PKC_PHOSPHO_SITE 329-331;	RRM 109-206; RRM 261-337; rrm 263-330; rrm 110-205; RRM 262-331; ANTIFREEZEI 221-232; hnRNP-L_PTB 106-445; ANTIFREEZEI 238-247;
DEX0450-032.orf.2	N	0 - 01-304;	41-60, 1.13; 19-27, 1.08; 176-195, 1.153; 223-234, 1.074; 4-12, 1.065; 76-86, 1.126; 263-271, 1.055; 255-261, 1.05; 88-102, 1.11; 236-245, 1.073; 152-171, 1.121; 109-144, 1.18;	PKC_PHOSPHO_SITE 14-16; RGD 290-292; MYRISTYL 285-290; CK2_PHOSPHO_SITE 294-297; CK2_PHOSPHO_SITE 205-208; MYRISTYL 13-18; TYR_PHOSPHO_SITE 114-122; PKC_PHOSPHO_SITE 181-183; MYRISTYL 103-108; PKC_PHOSPHO_SITE 281-283;	RRM 114-183; ANTIFREEZEI 90-99; ANTIFREEZEI 73-84; rrm 115-182; RRM 113-189;
DEX0450-032.aa.3	Y	0 - 01-606;	536-543, 1.124; 324-343, 1.153; 373-379, 1.05; 35-60, 1.152; 576-592, 1.115; 121-140, 1.141; 5-17, 1.091; 102-119, 1.139; 224-234, 1.126; 151-158, 1.129; 189-208, 1.13; 166-173, 1.139; 434-446, 1.148;	MYRISTYL 251-256; MYRISTYL 563-568; PKC_PHOSPHO_SITE 93-95; PKC_PHOSPHO_SITE 9-11; PKC_PHOSPHO_SITE 575-577; PKC_PHOSPHO_SITE 20-22; MYRISTYL 44-49; PKC_PHOSPHO_SITE 61-63; MYRISTYL 60-65; PKC_PHOSPHO_SITE 329-331; CK2_PHOSPHO_SITE 461-464; MYRISTYL	hnRNP-L_PTB 106-546; RRM 262-331; RRM 109-206; RRM 261-337; rrm 110-205; rrm 263-330;

			257-292,1.18; 395-426,1.154; 236-250,1.11; 300-319,1.121; 69-76,1.138; 448-520,1.174; 550-565,1.144; 26-32,1.049;	163-168; PKC_PHOSPHO_SITE 381-383; PKC_PHOSPHO_SITE 458-460; ASN_GLYCOSYLATION 482-485; CK2_PHOSPHO_SITE 120-123; CK2_PHOSPHO_SITE 353-356; CAMP_PHOSPHO_SITE 62-65; MYRISTYL 128-133; TYR_PHOSPHO_SITE 262-270; PKC_PHOSPHO_SITE 501-503; MYRISTYL 523-528; MYRISTYL 467-472; CK2_PHOSPHO_SITE 20-23; ASN_GLYCOSYLATION 91-94; MYRISTYL 396-401; PKC_PHOSPHO_SITE 414-416; MYRISTYL 556-561; PKC_PHOSPHO_SITE 389-391;	
DEX0450-032.orf.3	N	0 - ol-227;	76-86,1.126; 4-12,1.065; 41-60,1.13; 19-27,1.08; 88-102,1.11; 109-144,1.18; 152-171,1.121; 176-195,1.153;	PKC_PHOSPHO_SITE 14-16; MYRISTYL 103-108; PKC_PHOSPHO_SITE 181-183; TYR_PHOSPHO_SITE 114-122; CK2_PHOSPHO_SITE 205-208; MYRISTYL 13-18;	RRM 113-189; ANTIFREEZEI 73-84; ANTIFREEZEI 90-99; rrm 115-182; RRM 114-183;
DEX0450-032.aa.4	Y	0 - ol-432;	224-234,1.126; 189-208,1.13; 69-76,1.138; 300-319,1.121; 373-409,1.139; 151-160,1.165; 102-119,1.139; 257-292,1.18; 167-175,1.08; 26-32,1.049; 324-343,1.153; 5-17,1.091; 121-140,1.141; 236-250,1.11; 35-60,1.152; 412-421,1.186;	PKC_PHOSPHO_SITE 61-63; PKC_PHOSPHO_SITE 162-164; PKC_PHOSPHO_SITE 329-331; MYRISTYL 251-256; CK2_PHOSPHO_SITE 20-23; PKC_PHOSPHO_SITE 93-95; MYRISTYL 153-158; MYRISTYL 44-49; CAMP_PHOSPHO_SITE 62-65; MYRISTYL 128-133; MYRISTYL 60-65; PKC_PHOSPHO_SITE 20-22; MYRISTYL 161-166; PKC_PHOSPHO_SITE 9-11; TYR_PHOSPHO_SITE 262-270; CK2_PHOSPHO_SITE 120-123; MYRISTYL 410-415; CK2_PHOSPHO_SITE 353-356; MYRISTYL 407-412; ASN_GLYCOSYLATION 91-94;	HOMSERKINASE 242-257; HOMSERKINASE 403-418; RRM 109-206; rrm 263-330; rrm 110-205; ANTIFREEZEI 238-247; ALA_RICH 371-411; ANTIFREEZEI 221-232; hnRNP-L_PTB 106-432; KV14CHANNEL 392-402; KV14CHANNEL 405-414; RRM 261-337; RRM 262-331;
DEX0450-032.orf.	N	0 - ol-284;	225-261,1.139; 152-171,1.121; 4-12,1.065; 176-	MYRISTYL 13-18; PKC_PHOSPHO_SITE 181-183; MYRISTYL 262-267;	HOMSERKINASE 94-109; ANTIFREEZEI 90-99;

4				195, 1.153; 109-144, 1.18; 19-27, 1.08; 76-86, 1.126; 264-273, 1.186; 88-102, 1.11; 41-60, 1.13;	CK2_PHOSPHO_SITE 205-208; TYR_PHOSPHO_SITE 114-122; PKC_PHOSPHO_SITE 14-16; MYRISTYL 103-108; MYRISTYL 259-264;	HOMSERKINASE 255-270; ALA_RICH 223-263; ANTIFREEZEI 73-84; rrm 115-182; RRM 113-189; KV14CHANNEL 257-266; KV14CHANNEL 244-254; RRM 114-183;
DEX0450- 032.orf. 5	N	0 - 01- 304;	152-171, 1.121; 88-102, 1.11; 19-27, 1.08; 109-144, 1.18; 76-86, 1.126; 236-245, 1.073; 176-195, 1.153; 255- 261, 1.05; 41-60, 1.13; 263- 271, 1.055; 223-234, 1.074; 4-12, 1.065;	MYRISTYL 285-290; PKC_PHOSPHO_SITE 14-16; MYRISTYL 103-108; MYRISTYL 13-18; PKC_PHOSPHO_SITE 181-183; RGD 290-292; CK2_PHOSPHO_SITE 205-208; CK2_PHOSPHO_SITE 294-297; TYR_PHOSPHO_SITE 114-122; PKC_PHOSPHO_SITE 281-283;	RRM 114-183; ANTIFREEZEI 73-84; ANTIFREEZEI 90-99; rrm 115-182; RRM 113-189;	
DEX0450- 032.orf. 6	N	0 - 01- 304;	109-144, 1.18; 176- 195, 1.153; 88-102, 1.11; 263-271, 1.055; 236- 245, 1.073; 19-27, 1.08; 41- 60, 1.13; 255-261, 1.05; 223- 234, 1.074; 152-171, 1.121; 76-86, 1.126; 4-12, 1.065;	PKC_PHOSPHO_SITE 281-283; MYRISTYL 103-108; RGD 290-292; PKC_PHOSPHO_SITE 14-16; PKC_PHOSPHO_SITE 181-183; MYRISTYL 285-290; MYRISTYL 13-18; CK2_PHOSPHO_SITE 205-208; TYR_PHOSPHO_SITE 114-122; CK2_PHOSPHO_SITE 294-297;	RRM 113-189; RRM 114- 183; ANTIFREEZEI 90-99; rrm 115-182; ANTIFREEZEI 73-84;	
DEX0450- 032.orf. 7	N	0 - 01- 304;	255-261, 1.05; 88-102, 1.11; 152-171, 1.121; 76-86, 1.126; 176-195, 1.153; 19-27, 1.08; 236-245, 1.073; 263- 271, 1.055; 4-12, 1.065; 223- 234, 1.074; 109-144, 1.18; 41-60, 1.13;	MYRISTYL 13-18; CK2_PHOSPHO_SITE 205-208; PKC_PHOSPHO_SITE 14-16; RGD 290-292; MYRISTYL 285-290; MYRISTYL 103-108; PKC_PHOSPHO_SITE 281-283; CK2_PHOSPHO_SITE 294-297; PKC_PHOSPHO_SITE 181-183; TYR_PHOSPHO_SITE 114-122; TYR_PHOSPHO_SITE 114-122;	rrm 115-182; RRM 114- 183; ANTIFREEZEI 90-99; RRM 113-189; ANTIFREEZEI 73-84;	
DEX0450- 033.aa.1	N	0 - 01- 315;	231-237, 1.068; 208- 213, 1.081; 4-23, 1.174; 112- 125, 1.087; 171-194, 1.127; 39-62, 1.133; 144-167, 1.086; 69-75, 1.05;	MYRISTYL 64-69; CK2_PHOSPHO_SITE 274-277; MYRISTYL 85-90; CK2_PHOSPHO_SITE 9-12; PKC_PHOSPHO_SITE 77-79; MYRISTYL 93- 98; CK2_PHOSPHO_SITE 110-113; CK2_PHOSPHO_SITE 249-252; MYRISTYL 81-86; PKC_PHOSPHO_SITE 268-270;	TYPE2KERATIN 178-191; TYPE2KERATIN 106-114; SER_RICH 9-77; TYPE1KERATIN 181-194; TYPE1KERATIN 202-225; TYPE2KERATIN 192-211; filament 103-311;	

				CK2_PHOSPHO_SITE 117-120; CK2_PHOSPHO_SITE 297-300; MYRISTYL 80-85; CK2_PHOSPHO_SITE 225-228; ASN_GLYCOSYLATION 217-220; MYRISTYL 90-95; MYRISTYL 306-311; MYRISTYL 67-72; MYRISTYL 62-67; MYRISTYL 86- 91; PKC_PHOSPHO_SITE 28-30; PKC_PHOSPHO_SITE 274-276; MYRISTYL 99-104;	
DEX0450- 033.orf. 1	N	0 - ol- 296;		PKC_PHOSPHO_SITE 77-79; CK2_PHOSPHO_SITE 277-280; MYRISTYL 85-90; MYRISTYL 86-91; MYRISTYL 62- 67; CK2_PHOSPHO_SITE 110-113; CK2_PHOSPHO_SITE 272-275; MYRISTYL 80-85; PKC_PHOSPHO_SITE 277-279; CK2_PHOSPHO_SITE 225-228; MYRISTYL 67-72; MYRISTYL 247-252; CK2_PHOSPHO_SITE 9-12; MYRISTYL 64- 69; CK2_PHOSPHO_SITE 257-260; MYRISTYL 81-86; ASN_GLYCOSYLATION 217-220; MYRISTYL 90-95; MYRISTYL 99-104; TYR_PHOSPHO_SITE 238-245; MYRISTYL 93-98; CK2_PHOSPHO_SITE 117-120; PKC_PHOSPHO_SITE 28-30; MYRISTYL 57-62; ASN_GLYCOSYLATION 256-259; CK2_PHOSPHO_SITE 93-96; MYRISTYL 38-43; MYRISTYL 75-80; ASN_GLYCOSYLATION 193-196; MYRISTYL 66-71; PKC_PHOSPHO_SITE 4-6; MYRISTYL 61-66; CK2_PHOSPHO_SITE 86- 89; MYRISTYL 56-61; MYRISTYL 62-67; CK2_PHOSPHO_SITE 201-204; PKC_PHOSPHO_SITE 264-266; MYRISTYL 43-48; MYRISTYL 40-45; MYRISTYL 232- 237; CK2_PHOSPHO_SITE 231-234; PKC_PHOSPHO_SITE 53-55; MYRISTYL 69-	filament 103-291; TYPE2KERATIN 106-114; TYPE1KERATIN 181-194; TYPE2KERATIN 192-211; TYPE2KERATIN 178-191; TYPE1KERATIN 202-225; SER_RICH 9-77;
DEX0450- 033.aa.2	N	0 - ol- 267;	45-51,1.05; 124-143,1.086; 147-154,1.127; 16-38,1.133; 222-232,1.082; 160- 167,1.03; 207-213,1.068; 88-101,1.087; 239- 244,1.085;		TYPE2KERATIN 154-167; TYPE2KERATIN 168-187; filament 79-266; TYPE1KERATIN 178-201; TYPE1KERATIN 157-170; TYPE2KERATIN 82-90;

DEX0450-033.orf.2	N	0 - 01-454;	<p>40-62, 1.133; 324-333, 1.082; 8-24, 1.263; 231-237, 1.068; 246-264, 1.101; 266-273, 1.041; 184-191, 1.03; 69-75, 1.05; 171-178, 1.127; 148-167, 1.086; 112-125, 1.087; 386-402, 1.115; 302-314, 1.096; 363-372, 1.124; 439-445, 1.139; 350-359, 1.092;</p>	<p>74; CK2_PHOSPHO_SITE 225-228; TYR_PHOSPHO_SITE 286-294; MYRISTYL 24-29; PKC_PHOSPHO_SITE 336-338; ASN GLYCOSYLATION 7-10; CK2_PHOSPHO_SITE 319-322; MYRISTYL 86-91; CK2_PHOSPHO_SITE 110-113; MYRISTYL 99-104; TYR_PHOSPHO_SITE 396-404; CK2_PHOSPHO_SITE 117-120; MYRISTYL 64-69; MYRISTYL 93-98; MYRISTYL 85-90; MYRISTYL 314-319; MYRISTYL 380-385; MYRISTYL 80-85; ASN GLYCOSYLATION 217-220; PKC_PHOSPHO_SITE 433-435; PKC_PHOSPHO_SITE 403-405; PKC_PHOSPHO_SITE 347-349; MYRISTYL 67-72; MYRISTYL 81-86; CK2_PHOSPHO_SITE 347-350; ASN GLYCOSYLATION 447-450; PKC_PHOSPHO_SITE 28-30; CK2_PHOSPHO_SITE 376-379; TYR_PHOSPHO_SITE 349-355; MYRISTYL 62-67; PKC_PHOSPHO_SITE 77-79; MYRISTYL 90-95; PKC_PHOSPHO_SITE 434-436;</p>	<p>TYPE2KERATIN 178-191; TYPE2KERATIN 106-114; TYPE1KERATIN 257-277; IF 401-409; TYPE1KERATIN 329-344; TYPE1KERATIN 355-381; filament 103-415; TYPE1KERATIN 181-194; TYPE1KERATIN 202-225; TYPE2KERATIN 192-211;</p>
DEX0450-034.aa.1	N	0 - 01-104;	<p>5-12, 1.07; 39-46, 1.064; 64-101, 1.148;</p>	<p>CK2_PHOSPHO_SITE 17-20; PKC_PHOSPHO_SITE 14-16; ASN GLYCOSYLATION 60-63; MYRISTYL 49-54;</p>	<p>TYPE2KERATIN 3-15; TYPE2KERATIN 48-61;</p>
DEX0450-035.aa.1	N	0 - 01-768;	<p>496-513, 1.103; 269-281, 1.132; 67-77, 1.072; 606-611, 1.067; 759-765, 1.083; 419-426, 1.104; 585-601, 1.125; 618-623, 1.045; 439-446, 1.119; 125-136, 1.043; 534-</p>	<p>MYRISTYL 22-27; MYRISTYL 706-711; MYRISTYL 271-276; MYRISTYL 447-452; PKC_PHOSPHO_SITE 492-494; PKC_PHOSPHO_SITE 48-50; CAMP_PHOSPHO_SITE 61-64; MYRISTYL 668-673; CK2_PHOSPHO_SITE 596-599; MYRISTYL 368-373; MYRISTYL 686-691;</p>	<p>ADENYLKINASE 603-617; SPRY 288-406; ATP_GTP_A 447-454; GLY_RICH 646-737; ADENYLKINASE 444-457; ATP_GTP_A 142-149; SPRY 274-406; SPRY 274-406;</p>

			<p>541,1.114; 348-354,1.125; 214-219,1.076; 521- 530,1.068; 152-164,1.163; 692-704,1.1; 572-578,1.138; 359-365,1.093; 407- 417,1.075; 284-297,1.141; 544-553,1.231; 10-21,1.128; 321-335,1.08; 27-46,1.178; 299-305,1.062; 227- 244,1.195; 48-54,1.032; 370-401,1.222;</p>	<p>MYRISTYL 717-722; PKC PHOSPHO_SITE 709-711; PKC PHOSPHO_SITE 560-562; ASN GLYCOSYLATION 582-585; CK2_PHOSPHO_SITE 584-587; PKC_PHOSPHO_SITE 633-635; CK2_PHOSPHO_SITE 475-478; ASN GLYCOSYLATION 636-639; MYRISTYL 664-669; MYRISTYL 164-169; PKC PHOSPHO_SITE 638-640; MYRISTYL 328-333; MYRISTYL 751-756; ASN GLYCOSYLATION 526-529; MYRISTYL 3-8; MYRISTYL 665-670; ASN GLYCOSYLATION 740-743; MYRISTYL 733-738; CK2_PHOSPHO_SITE 90-93; MYRISTYL 25-30; MYRISTYL 629-634; MYRISTYL 312-317; PKC PHOSPHO_SITE 616-618; MYRISTYL 168-173; MYRISTYL 647-652; MYRISTYL 683-688; PKC PHOSPHO_SITE 76-78; PKC PHOSPHO_SITE 325-327; MYRISTYL 687-692; MYRISTYL 660-665; PKC PHOSPHO_SITE 630-632; MYRISTYL 685-690; MYRISTYL 265-270; PKC PHOSPHO_SITE 284-286; MYRISTYL 450-455; MYRISTYL 684-689; PKC PHOSPHO_SITE 81-83;</p>				
DEX0450- 035.orf. 1	N	0 - 01- 793;	<p>236-244,1.076; 294- 306,1.132; 373-379,1.125; 36-44,1.103; 631-636,1.067; 252-269,1.195; 546- 556,1.068; 643-648,1.045; 395-426,1.222; 464- 471,1.119; 559-566,1.114; 717-729,1.1; 73-79,1.032; 569-578,1.231; 444- 452,1.104; 521-538,1.103; 4-15.1.069; 52-71.1.178;</p>	<p>MYRISTYL 50-55; MYRISTYL 353-358; MYRISTYL 393-398; MYRISTYL 776-781; PKC PHOSPHO_SITE 106-108; PKC PHOSPHO_SITE 517-519; PKC PHOSPHO_SITE 655-657; PKC PHOSPHO_SITE 350-352; CK2_PHOSPHO_SITE 621-624; ASN GLYCOSYLATION 607-610; MYRISTYL 21-26; MYRISTYL 689-694; MYRISTYL 15-20; PKC PHOSPHO_SITE 734-736; MYRISTYL 25-30; MYRISTYL 193-198;</p>	<p>ADENYLTKINASE 628-642; GLY_RICH 671-762; SPRY 299-431; SPRY 299-431; SPRY 313-431; ADENYLTKINASE 469-482; ATP_GTP_A 472-479; ATP_GTP_A 167-174;</p>			

			324-332,1.062; 150-161,1.043; 597-604,1.138; 610-626,1.125; 384-390,1.093; 346-360,1.08; 309-322,1.141; 784-790,1.083; 92-102,1.072; 177-189,1.163; 432-442,1.075;	MYRISTYL 709-714; CAMP_PHOSPHO_SITE 86-89; MYRISTYL 742-747; ASN_GLYCOSYLATION 551-554; MYRISTYL 290-295; MYRISTYL 685-690; PKC_PHOSPHO_SITE 663-665; MYRISTYL 711-716; ASN_GLYCOSYLATION 765-768; MYRISTYL 731-736; MYRISTYL 693-698; MYRISTYL 189-194; CK2_PHOSPHO_SITE 609-612; MYRISTYL 758-763; MYRISTYL 690-695; PKC_PHOSPHO_SITE 101-103; ASN_GLYCOSYLATION 661-664; MYRISTYL 710-715; PKC_PHOSPHO_SITE 309-311; MYRISTYL 708-713; CK2_PHOSPHO_SITE 500-503; MYRISTYL 337-342; MYRISTYL 712-717; PKC_PHOSPHO_SITE 585-587; MYRISTYL 7-12; MYRISTYL 672-677; CK2_PHOSPHO_SITE 115-118; MYRISTYL 472-477; MYRISTYL 654-659; MYRISTYL 296-301; PKC_PHOSPHO_SITE 658-660; MYRISTYL 475-480; PKC_PHOSPHO_SITE 73-75; PKC PHOSPHO SITE 641-643;		
DEX0450-036.aa.1	N	0 - ol-325;	152-159,1.096; 4-38,1.178; 105-128,1.122; 188-198,1.097; 262-277,1.145; 165-174,1.106; 242-250,1.118; 55-76,1.156; 219-224,1.06;	TYR_PHOSPHO_SITE 102-110; PKC_PHOSPHO_SITE 276-278; ASN_GLYCOSYLATION 260-263; CK2_PHOSPHO_SITE 221-224; TYR_PHOSPHO_SITE 201-207; CK2_PHOSPHO_SITE 137-140; CK2_PHOSPHO_SITE 13-16;	sp_P34932_HS74_HUMAN 198-269; sp_Q92598_H105_HUMAN 42-169;	
DEX0450-037.aa.1	N	0 - il-131;	47-70,1.153; 73-84,1.132; 26-41,1.214; 10-20,1.057;	CK2_PHOSPHO_SITE 56-59; PKC_PHOSPHO_SITE 89-91; CK2_PHOSPHO_SITE 87-90; CK2_PHOSPHO_SITE 12-15; PKC_PHOSPHO_SITE 80-82;	sp_P18758_TYB4_XENLA 94-131; THY 94-130; THYMOSIN_B4 105-116; Thymosin 89-129;	
DEX0450-037.orf.1	N	0 - ol-116;	11-26,1.214; 32-55,1.153; 58-69,1.132;	CK2_PHOSPHO_SITE 41-44; PKC_PHOSPHO_SITE 1-3; PKC PHOSPHO SITE 65-67;	THYMOSIN_B4 90-101; sp_P18758_TYB4_XENLA 79-116: Thymosin 74-	

179

					CK2_PHOSPHO_SITE 72-75; PKC_PHOSPHO_SITE 74-76;	114; THY 79-115;
DEX0450- 038.aa.1	N	0 - ol- 63;	33-46,1.084; 16-25,1.113; 4-11,1.205; 48-60,1.193;		CK2_PHOSPHO_SITE 47-50; PKC_PHOSPHO_SITE 7-9;	
DEX0450- 038.orf. 1	N	0 - ol- 97;	4-27,1.171; 32-47,1.134; 49-59,1.215;			
DEX0450- 039.aa.1	N	0 - ol- 163;	106-113,1.134; 120- 132,1.156; 134-160,1.207; 15-25,1.122;		PKC_PHOSPHO_SITE 50-52; TYR_PHOSPHO_SITE 63-69; CK2_PHOSPHO_SITE 27-30; CK2_PHOSPHO_SITE 20-23; PKC_PHOSPHO_SITE 116-118; CK2_PHOSPHO_SITE 101-104; PKC_PHOSPHO_SITE 31-33; PKC PHOSPHO SITE 134-136;	Clathrin_lg_ch 1-145; sp_P09496_CLCA_HUMAN 1- 123;
DEX0450- 039.orf. 1	Y	0 - ol- 283;	227-234,1.134; 75-82,1.094; 25-44,1.186; 5-22,1.155; 95-100,1.052; 247- 257,1.142; 263-280,1.207; 136-146,1.122; 47-55,1.039;		MYRISTYL 113-118; CK2_PHOSPHO_SITE 222-225; PKC_PHOSPHO_SITE 253-255; MYRISTYL 3-8; CK2_PHOSPHO_SITE 141- 144; MYRISTYL 120-125; MYRISTYL 23- 28; PKC_PHOSPHO_SITE 171-173; MYRISTYL 63-68; CK2_PHOSPHO_SITE 148-151; MYRISTYL 51-56; MYRISTYL 25-30; PKC PHOSPHO_SITE 152-154; TYR_PHOSPHO_SITE 184-190; PKC_PHOSPHO_SITE 237-239; MYRISTYL 65-70;	CLATHRIN_LIGHT_CHN_2 242-255; sp_P09496_CLCA_HUMAN 71-257; Clathrin_lg_ch 46-260; CLATHRIN_LIGHT_CHN_1 78-84;
DEX0450- 039.aa.2	N	0 - ol- 222;	82-93,1.122; 174-181,1.134; 52-58,1.052; 32-41,1.094; 4-12,1.039; 188-202,1.156;		ASN_GLYCOSYLATION 216-219; MYRISTYL 8-13; PKC PHOSPHO_SITE 202-204; PKC PHOSPHO_SITE 68-70; MYRISTYL 215-220; TYR PHOSPHO_SITE 131-137; CK2_PHOSPHO_SITE 88-91; MYRISTYL 22- 27; PKC PHOSPHO_SITE 99-101; PKC PHOSPHO_SITE 184-186; CK2_PHOSPHO_SITE 95-98; MYRISTYL 20- 25; CK2_PHOSPHO_SITE 169-172; PKC PHOSPHO_SITE 118-120;	sp_P09496_CLCA_HUMAN 28-191; CLATHRIN_LIGHT_CHN_1 35-41; Clathrin_lg_ch 3-203;

DEX0450- 039.orf. 2	Y	0 - 01- 250;	125-135,1.122; 216- 223,1.134; 236-247,1.142; 5-14,1.175; 16-61,1.224;	PKC_PHOSPHO_SITE 226-228; PKC_PHOSPHO_SITE 78-80; PKC_PHOSPHO_SITE 110-112; TYR_PHOSPHO_SITE 173-179; CK2_PHOSPHO_SITE 137-140; PKC_PHOSPHO_SITE 81-83; PKC_PHOSPHO_SITE 141-143; CK2_PHOSPHO_SITE 130-133; CK2_PHOSPHO_SITE 211-214; PKC_PHOSPHO_SITE 160-162; ASN_GLYCOSYLATION 1-4; PKC_PHOSPHO_SITE 242-244; PKC_PHOSPHO_SITE 91-93;	CLATHRIN_LIGHT_CHN_2 231-244; Clathrin_lg_ch 49-249; sp_P09496_CLCA_HUMAN 94-248;
DEX0450- 039.aa.3	N	0 - 01- 142;	127-134,1.06; 86-93,1.094; 16-33,1.186; 106-112,1.052; 58-66,1.039; 36-55,1.186;	MYRISTYL 62-67; AMIDATION 137-140; PKC_PHOSPHO_SITE 133-135; CAMP_PHOSPHO_SITE 134-137; PKC_PHOSPHO_SITE 137-139; MYRISTYL 76-81; MYRISTYL 34-39; PKC_PHOSPHO_SITE 1-3; MYRISTYL 74- 79; MYRISTYL 36-41; PKC_PHOSPHO_SITE 122-124;	CLATHRIN_LIGHT_CHN_1 89-95; sp_P08081_CLCA_RAT 82- 117;
DEX0450- 039.orf. 3	N	0 - 01- 220;	36-55,1.186; 106-111,1.052; 16-33,1.186; 58-66,1.039; 86-93,1.094; 186-193,1.134; 206-217,1.142;	CK2_PHOSPHO_SITE 181-184; MYRISTYL 62-67; TYR_PHOSPHO_SITE 143-149; PKC_PHOSPHO_SITE 196-198; MYRISTYL 34-39; MYRISTYL 124-129; PKC_PHOSPHO_SITE 212-214; PKC_PHOSPHO_SITE 130-132; MYRISTYL 36-41; MYRISTYL 76-81; MYRISTYL 74- 79; PKC_PHOSPHO_SITE 1-3;	sp_O08585_CLCA_MOUSE 127-218; CLATHRIN_LIGHT_CHN_1 89-95; CLATHRIN_LIGHT_CHN_2 201-214; Clathrin_lg_ch 57-219;
DEX0450- 039.aa.4	N	0 - 01- 111;	87-105,1.126; 14-25,1.122;	CK2_PHOSPHO_SITE 20-23; CK2_PHOSPHO_SITE 27-30; PKC_PHOSPHO_SITE 105-107; TYR_PHOSPHO_SITE 63-69; PKC_PHOSPHO_SITE 50-52; TYR_PHOSPHO_SITE 84-91; PKC_PHOSPHO_SITE 31-33; MYRISTYL	sp_P09496_CLCA_HUMAN 1- 102; Clathrin_lg_ch 1- 111;

				104-109;	
DEX0450- 039.orf. 4	Y	0 - ol- 236;	29-48,1.186; 5-26,1.186; 216-230,1.126; 79-86,1.094; 99-104,1.052; 51-59,1.039; 140-150,1.122;	TYR_PHOSPHO_SITE 188-194; PKC_PHOSPHO_SITE 230-232; MYRISTYL 29-34; MYRISTYL 69-74; TYR_PHOSPHO_SITE 209-216; MYRISTYL 124-129; CK2_PHOSPHO_SITE 145-148; MYRISTYL 229-234; PKC_PHOSPHO_SITE 156-158; MYRISTYL 117-122; MYRISTYL 27-32; CK2_PHOSPHO_SITE 152-155; PKC_PHOSPHO_SITE 175-177; MYRISTYL 55-60; MYRISTYL 67-72; MYRISTYL 203-208; CK2_PHOSPHO_SITE 101-104; PKC_PHOSPHO_SITE 50-52; AMIDATION 181-184; CK2_PHOSPHO_SITE 27-30; PKC_PHOSPHO_SITE 134-136; AMIDATION 184-187; CK2_PHOSPHO_SITE 20-23; PKC_PHOSPHO_SITE 116-118; PKC_PHOSPHO_SITE 31-33; AMIDATION 195-198; TYR_PHOSPHO_SITE 63-69; PKC PHOSPHO SITE 181-183; MYRISTYL 27-32; PKC PHOSPHO_SITE 156-158; MYRISTYL 69-74; MYRISTYL 29-34; CK2 PHOSPHO_SITE 152-155; PKC PHOSPHO SITE 241-243; MICROBODIES_CTER 261-263; CK2 PHOSPHO_SITE 226-229; MYRISTYL 55-60; MYRISTYL 124-129; PKC PHOSPHO_SITE 175-177; TYR_PHOSPHO_SITE 188-194; MYRISTYL 67-72; MYRISTYL 117-122; PKC PHOSPHO_SITE 257-259; CK2 PHOSPHO_SITE 145-148; PKC PHOSPHO_SITE 50-52; PKC_PHOSPHO_SITE 131-133; PKC_PHOSPHO_SITE 116-118; CK2 PHOSPHO SITE 27-30;	Clathrin_lg_ch 50-236; sp_P09496_CLCA_HUMAN 75-227; CLATHRIN_LIGHT_CHN_1 82-88;
DEX0450- 039.aa.5	N	0 - ol- 211;	146-178,1.243; 201- 208,1.162; 120-132,1.156; 106-113,1.134; 15-25,1.122;	Clathrin_lg_ch 1-135; sp_P09496_CLCA_HUMAN 1- 123;	
DEX0450- 039.orf. 5	Y	0 - ol- 263;		CLATHRIN_LIGHT_CHN_1 82-88; CLATHRIN_LIGHT_CHN_2 246-259; sp_P09496_CLCA_HUMAN 75-261; Clathrin_lg_ch 50-261;	
DEX0450- 039.aa.6	N	0 - ol- 150;	119-127,1.056; 132- 147,1.204; 15-25,1.122; 106-113,1.134;	Clathrin_lg_ch 1-145; sp_P09496_CLCA_HUMAN 1- 121;	

					CK2_PHOSPHO_SITE 101-104; PKC_PHOSPHO_SITE 117-119; TYR_PHOSPHO_SITE 63-69; PKC_PHOSPHO_SITE 130-132; CK2_PHOSPHO_SITE 20-23; PKC_PHOSPHO_SITE 31-33;		
DEX0450_039.orf.6	Y	0 - ol-269;	29-48,1.186; 244-254,1.069; 257-266,1.185; 79-86,1.094; 99-104,1.052; 51-59,1.039; 231-238,1.134; 5-26,1.186; 140-150,1.122;		TYR_PHOSPHO_SITE 188-194; MYRISTYL 55-60; PKC_PHOSPHO_SITE 241-243; MYRISTYL 117-122; PKC_PHOSPHO_SITE 156-158; MYRISTYL 69-74; CK2_PHOSPHO_SITE 226-229; MYRISTYL 67-72; PKC_PHOSPHO_SITE 255-257; MYRISTYL 124-129; CK2_PHOSPHO_SITE 152-155; PKC_PHOSPHO_SITE 175-177; CK2_PHOSPHO_SITE 145-148; MYRISTYL 27-32; PKC_PHOSPHO_SITE 242-244; MYRISTYL 29-34; PKC_PHOSPHO_SITE 256-258;	Clathrin_lg_ch 50-261; sp_P09496_CLCA_HUMAN 75-246; CLATHRIN_LIGHT_CHN_1 82-88;	
DEX0450_040.aa.1	Y	0 - ol-152;	131-149,1.148; 108-121,1.158; 4-30,1.234; 72-78,1.044; 89-105,1.181; 45-51,1.067;		MYRISTYL 40-45; PKC_PHOSPHO_SITE 29-31; MYRISTYL 90-95;	LYSOZYME 20-38; LYZLACT 21-31; LYZLACT 123-134; LYSOZYME 89-99; LYZLACT 69-85; LACTALBUMIN 122-131; LYSOZYME 100-115; LACTALBUMIN 100-111; LYSOZYME 122-131; LACTALBUMIN_LYSOZYME 95-113; LACTALBUMIN 27-47; LYZ1 19-143; LYZLACT 41-50; Lys 19-142; LYZLACT 93-102; LYSOZYME 51-63; LYZLACT 103-118;	
DEX0450_041.aa.1	N	5 - ol-28;tm29-46;i47-57:tm58-	141-175,1.216; 58-105,1.201; 113-131,1.153; 15-49,1.224;		CAMP_PHOSPHO_SITE 172-175; MYRISTYL 150-155; MYRISTYL 14-19; CK2_PHOSPHO_SITE 80-83; MYRISTYL 122-127; AMIDATION 170-173;	ERLUMENR 122-140; ERLUMENR 150-165; ER_lumen_recept 31-168; so_099JH8 099JH8 MOUSE	

		75; o76-84; tm85-104; i105-116; tm117-134; o135-143; tm144-166; i167-178;		PKC_PHOSPHO_SITE 58-60; MYRISTYL 9-14; MYRISTYL 54-59;	71-178; ERLUMENR 86-106; ER_LUMEN_RECEPTOR_2 92-101; ERLUMENR 108-122;
DEX0450-041.orf.1	N	0 - o1-183;	76-90, 1.167; 126-147, 1.158; 36-73, 1.211; 7-26, 1.168; 162-172, 1.186; 98-112, 1.187;	PKC PHOSPHO_SITE 90-92; PKC_PHOSPHO_SITE 113-115; CK2_PHOSPHO_SITE 151-154;	
DEX0450-042.aa.1	N	0 - o1-742;	144-163, 1.095; 6-21, 1.176; 104-119, 1.109; 238-300, 1.255; 187-196, 1.107; 530-544, 1.055; 47-57, 1.112; 200-209, 1.03; 384-391, 1.114; 353-364, 1.092; 643-649, 1.039; 394-399, 1.026; 217-225, 1.027; 61-68, 1.052; 27-33, 1.05; 493-505, 1.11; 615-624, 1.174; 331-345, 1.109; 729-737, 1.119; 433-462, 1.09; 72-78, 1.061; 702-707, 1.073;	PKC PHOSPHO_SITE 625-627; PKC_PHOSPHO_SITE 426-428; MYRISTYL 723-728; CK2 PHOSPHO_SITE 91-94; ASN GLYCOSYLATION 46-49; CK2_PHOSPHO_SITE 49-52; MYRISTYL 270-275; MYRISTYL 727-732; PKC PHOSPHO_SITE 712-714; CK2_PHOSPHO_SITE 564-567; CK2_PHOSPHO_SITE 512-515; CK2_PHOSPHO_SITE 176-179; PKC PHOSPHO_SITE 61-63; CK2_PHOSPHO_SITE 368-371; PKC PHOSPHO_SITE 487-489; PKC PHOSPHO_SITE 192-194; MYRISTYL 508-513; PKC PHOSPHO_SITE 724-726; CK2_PHOSPHO_SITE 404-407; CK2_PHOSPHO_SITE 314-317; MYRISTYL 114-119; CAMP PHOSPHO_SITE 662-665; PKC PHOSPHO_SITE 493-495; CK2_PHOSPHO_SITE 86-89; PKC PHOSPHO_SITE 551-553; CK2 PHOSPHO_SITE 606-609;	PRICHEXTENSIN 189-201; HISTONEH5 708-727; PRICHEXTENSIN 328-345; TREACLE 364-377; PRICHEXTENSIN 420-445; SER_RICH_2 364-569; SER_RICH_1 217-231; TREACLE 158-176; TREACLE 385-408; SRP40_C 644-739; HISTONEH5 612-636; HISTONEH5 547-568;

				CK2_PHOSPHO_SITE 41-44; PKC_PHOSPHO_SITE 481-483; CAMP_PHOSPHO_SITE 305-308; CK2_PHOSPHO_SITE 315-318; CK2_PHOSPHO_SITE 133-136; ASN_GLYCOSYLATION 561-564; PKC_PHOSPHO_SITE 304-306; CK2_PHOSPHO_SITE 313-316; CK2_PHOSPHO_SITE 274-277; MYRISTYL 267-272; CK2_PHOSPHO_SITE 231-234; CK2_PHOSPHO_SITE 467-470; PKC_PHOSPHO_SITE 437-439; CK2_PHOSPHO_SITE 226-229; CK2_PHOSPHO_SITE 563-566; CK2_PHOSPHO_SITE 376-379; CK2_PHOSPHO_SITE 476-479; ASN_GLYCOSYLATION 590-593; PKC_PHOSPHO_SITE 392-394; CK2_PHOSPHO_SITE 375-378; CK2_PHOSPHO_SITE 227-230; CK2_PHOSPHO_SITE 519-522; CK2_PHOSPHO_SITE 521-524; CK2_PHOSPHO_SITE 174-177; CAMP_PHOSPHO_SITE 721-724; CK2_PHOSPHO_SITE 175-178; CK2_PHOSPHO_SITE 514-517; CK2_PHOSPHO_SITE 413-416; CK2_PHOSPHO_SITE 168-171; ASN_GLYCOSYLATION 59-62; CK2_PHOSPHO_SITE 309-312; PKC_PHOSPHO_SITE 431-433; CK2_PHOSPHO_SITE 84-87; CK2_PHOSPHO_SITE 520-523; PKC_PHOSPHO_SITE 248-250; PKC_PHOSPHO_SITE 461-463; MYRISTYL 425-430; PKC_PHOSPHO_SITE 239-241; CK2_PHOSPHO_SITE 128-131;
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					CAMP_PHOSPHO_SITE 81-84; CK2_PHOSPHO_SITE 364-367; PKC_PHOSPHO_SITE 528-530; CK2_PHOSPHO_SITE 409-412; CK2_PHOSPHO_SITE 134-137; CK2_PHOSPHO_SITE 469-472; ASN_GLYCOSYLATION 429-432; CK2_PHOSPHO_SITE 475-478; CK2_PHOSPHO_SITE 569-572; CK2_PHOSPHO_SITE 170-173; CK2_PHOSPHO_SITE 474-477; MYRISTYL 543-548; CK2_PHOSPHO_SITE 92-95; PKC_PHOSPHO_SITE 718-720; CK2_PHOSPHO_SITE 414-417; CK2_PHOSPHO_SITE 308-311; CK2_PHOSPHO_SITE 129-132; CK2_PHOSPHO_SITE 374-377; PKC_PHOSPHO_SITE 581-583; PKC_PHOSPHO_SITE 736-738; CK2_PHOSPHO_SITE 568-571; CK2_PHOSPHO_SITE 468-471;			
DEX0450- 042.aa.2	N	0 - 01- 288;	4-10,1.142; 189-195,1.039; 248-253,1.073; 211- 216,1.044; 273-283,1.119; 161-170,1.174; 18-48,1.145; 76-90,1.055; 92-97,1.037;	CAMP_PHOSPHO_SITE 208-211; PKC_PHOSPHO_SITE 74-76; MYRISTYL 89- 94; CK2_PHOSPHO_SITE 58-61; CK2_PHOSPHO_SITE 110-113; ASN_GLYCOSYLATION 136-139; CK2_PHOSPHO_SITE 13-16; CK2_PHOSPHO_SITE 60-63; PKC_PHOSPHO_SITE 127-129; CK2_PHOSPHO_SITE 48-51; PKC_PHOSPHO_SITE 282-284; CK2_PHOSPHO_SITE 46-49; PKC_PHOSPHO_SITE 270-272; PKC_PHOSPHO_SITE 264-266; CK2_PHOSPHO_SITE 114-117; CK2_PHOSPHO_SITE 109-112; MYRISTYL 273-278; PKC_PHOSPHO_SITE 258-260;	HISTONEH5 254-273; HISTONEH5 192-206; HISTONEH5 93-114; HISTONEH5 158-182; SRP40_C 190-285; SER_RICH 40-115;			

186

DEX0450- 042.orf. 2	N	0 - 01- 265;	53-67,1.055; 188-193,1.044; 4-25,1.145; 166-172,1.039; 30-36,1.049; 69-75,1.037; 250-260,1.119; 138- 148,1.174; 225-231,1.073;	CK2_PHOSPHO_SITE 66-69; MYRISTYL 55- 60; PKC_PHOSPHO_SITE 171-173; CK2_PHOSPHO_SITE 152-155; ASN_GLYCOSYLATION 107-110; CK2_PHOSPHO_SITE 115-118; CK2_PHOSPHO_SITE 65-68; PKC_PHOSPHO_SITE 97-99; CAMP_PHOSPHO_SITE 267-270; MYRISTYL 269-274; CK2_PHOSPHO_SITE 67-70; MYRISTYL 246-251; PKC_PHOSPHO_SITE 259-261; PKC_PHOSPHO_SITE 235-237; PKC_PHOSPHO_SITE 51-53; PKC_PHOSPHO_SITE 241-243; CK2_PHOSPHO_SITE 91-94; PKC_PHOSPHO_SITE 247-249; MYRISTYL 66-71; CK2_PHOSPHO_SITE 92-95; CK2_PHOSPHO_SITE 25-28; MYRISTYL 32- 37; CK2_PHOSPHO_SITE 129-132; CK2_PHOSPHO_SITE 42-45; PKC_PHOSPHO_SITE 74-76; CK2_PHOSPHO_SITE 35-38; ASN_GLYCOSYLATION 113-116; CK2_PHOSPHO_SITE 87-90; ASN_GLYCOSYLATION 84-87; MYRISTYL 250-255; CK2_PHOSPHO_SITE 37-40; CAMP_PHOSPHO_SITE 244-247; CK2_PHOSPHO_SITE 2-5; CK2_PHOSPHO_SITE 44-47; PKC_PHOSPHO_SITE 104-106; CK2_PHOSPHO_SITE 43-46; PKC_PHOSPHO_SITE 148-150; CK2_PHOSPHO_SITE 86-89; CK2_PHOSPHO_SITE 23-26; CAMP_PHOSPHO_SITE 185-188;	CK2_PHOSPHO_SITE 66-69; MYRISTYL 55- 60; PKC_PHOSPHO_SITE 171-173; CK2_PHOSPHO_SITE 152-155; ASN_GLYCOSYLATION 107-110; CK2_PHOSPHO_SITE 115-118; CK2_PHOSPHO_SITE 65-68; PKC_PHOSPHO_SITE 97-99; CAMP_PHOSPHO_SITE 267-270; MYRISTYL 269-274; CK2_PHOSPHO_SITE 67-70; MYRISTYL 246-251; PKC_PHOSPHO_SITE 259-261; PKC_PHOSPHO_SITE 235-237; PKC_PHOSPHO_SITE 51-53; PKC_PHOSPHO_SITE 241-243; CK2_PHOSPHO_SITE 91-94; PKC_PHOSPHO_SITE 247-249; MYRISTYL 66-71; CK2_PHOSPHO_SITE 92-95; CK2_PHOSPHO_SITE 25-28; MYRISTYL 32- 37; CK2_PHOSPHO_SITE 129-132; CK2_PHOSPHO_SITE 42-45; PKC_PHOSPHO_SITE 74-76; CK2_PHOSPHO_SITE 35-38; ASN_GLYCOSYLATION 113-116; CK2_PHOSPHO_SITE 87-90; ASN_GLYCOSYLATION 84-87; MYRISTYL 250-255; CK2_PHOSPHO_SITE 37-40; CAMP_PHOSPHO_SITE 244-247; CK2_PHOSPHO_SITE 2-5; CK2_PHOSPHO_SITE 44-47; PKC_PHOSPHO_SITE 104-106; CK2_PHOSPHO_SITE 43-46; PKC_PHOSPHO_SITE 148-150; CK2_PHOSPHO_SITE 86-89; CK2_PHOSPHO_SITE 23-26; CAMP_PHOSPHO_SITE 185-188;		
DEX0450- 043.aa.1	N	6 - 01- 341:tm342	400-406,1.115; 338- 369,1.239; 88-110,1.146;	CK2_PHOSPHO_SITE 670-673; CK2_PHOSPHO_SITE 853-856;	SRP40_C 167-262; HISTONEH5 135-159; HISTONEH5 231-250; HISTONEH5 169-183; HISTONEH5 70-91; SER_RICH 17-92;		

			<p>588-593, 1.048; 1145-1158, 1.115; 790-818, 1.196; 1116-1138, 1.163; 55-63, 1.089; 720-735, 1.157; 1002-1016, 1.101; 1175-1218, 1.159; 256-266, 1.095; 268-301, 1.237; 188-205, 1.179; 529-546, 1.156; 854-876, 1.095; 612-659, 1.215; 235-253, 1.121; 946-951, 1.1; 464-506, 1.236; 129-148, 1.164; 509-523, 1.086; 889-896, 1.088; 898-932, 1.166; 415-457, 1.183; 578-585, 1.166; 825-845, 1.13; 30-50, 1.175; 306-315, 1.184; 19-26, 1.081; 1096-1109, 1.131; 217-229, 1.175; 1221-1228, 1.117; 1052-1087, 1.186; 150-158, 1.126; 4-9, 1.162; 978-1000, 1.174; 961-968, 1.082; 663-675, 1.207; 743-774, 1.125; 1021-1037, 1.137; 73-81, 1.18; 1258-1265, 1.058; 700-709, 1.094; 112-127, 1.127; 552-572, 1.144;</p>	<p>PKC_PHOSPHO_SITE 133-135; PKC_PHOSPHO_SITE 695-697; MYRISTYL 24-29; ASN_GLYCOSYLATION 131-134; CK2_PHOSPHO_SITE 227-230; CK2_PHOSPHO_SITE 369-372; CK2_PHOSPHO_SITE 459-462; MYRISTYL 142-147; PKC_PHOSPHO_SITE 368-370; CK2_PHOSPHO_SITE 373-376; MYRISTYL 707-712; ASN_GLYCOSYLATION 375-378; CK2_PHOSPHO_SITE 146-149; MYRISTYL 1017-1022; PKC_PHOSPHO_SITE 952-954; PKC_PHOSPHO_SITE 677-679; PKC_PHOSPHO_SITE 1090-1092; CK2_PHOSPHO_SITE 837-840; MYRISTYL 1170-1175; CAMP_PHOSPHO_SITE 957-960; PKC_PHOSPHO_SITE 960-962; PKC_PHOSPHO_SITE 889-891; ASN_GLYCOSYLATION 932-935; PKC_PHOSPHO_SITE 286-288; MYRISTYL 691-696; CK2_PHOSPHO_SITE 215-218; PKC_PHOSPHO_SITE 955-957; PKC_PHOSPHO_SITE 682-684; ASN_GLYCOSYLATION 323-326; ASN_GLYCOSYLATION 690-693; MYRISTYL 428-433; ASN_GLYCOSYLATION 190-193;</p>		
<p>364;i365-467;tm468 - 490;o491-518;tm519 - 541;i542-552;tm553 - 571;o572-625;tm626 - 648;i649-652;tm653 - 675;o676-1276;</p>		<p>254-288, 1.166; 19-31, 1.207; 4-15, 1.144; 99-130, 1.125; 334-356, 1.174; 181-201, 1.13; 614-621, 1.058; 472-494, 1.163; 210-232, 1.095; 317-324, 1.082; 531-574, 1.159; 358-372, 1.101; 245-252, 1.088; 501-514, 1.115; 302-307, 1.1;</p>	<p>PKC_PHOSPHO_SITE 6-8; PKC_PHOSPHO_SITE 446-448; PKC_PHOSPHO_SITE 38-40; MYRISTYL 373-378; PKC_PHOSPHO_SITE 308-310; CK2_PHOSPHO_SITE 209-212; MYRISTYL 526-531; CK2_PHOSPHO_SITE 26-29; CK2_PHOSPHO_SITE 193-196; PKC_PHOSPHO_SITE 33-35; MYRISTYL 47-52; CAMP_PHOSPHO_SITE 313-316;</p>	<p>1 - i1-8;tm9-31;o32-632;</p>	Y	DEX0450-043.orf.1

				76-91,1.157; 452-465,1.131; 377-393,1.137; 408- 443,1.186; 56-65,1.094; 146-174,1.196; 577- 584,1.117;	ASN_GLYCOSYLATION 288-291; PKC_PHOSPHO_SITE 51-53; PKC_PHOSPHO_SITE 311-313; ASN_GLYCOSYLATION 46-49; MYRISTYL 63-68; PKC_PHOSPHO_SITE 245-247; PKC_PHOSPHO_SITE 316-318;	
DEX0450- 044.aa.1	Y	0 - ol- 159;		120-125,1.058; 137- 151,1.11; 83-89,1.037; 4- 46,1.193; 98-107,1.055;	ASN_GLYCOSYLATION 94-97; PKC_PHOSPHO_SITE 96-98; CAMP_PHOSPHO_SITE 126-129; CK2_PHOSPHO_SITE 55-58; PKC_PHOSPHO_SITE 17-19; PKC_PHOSPHO_SITE 110-112; CAMP_PHOSPHO_SITE 19-22;	
DEX0450- 044.aa.2	N	3 - il- 71;tm72- 94;o95- 108;tm109 - 131;i132- 168;tm169 - 188;o189- 313;		237-243,1.037; 168- 200,1.193; 252-261,1.055; 41-51,1.164; 291-305,1.11; 160-165,1.057; 102- 115,1.197; 274-279,1.058; 72-96,1.297; 17-25,1.075; 117-137,1.293; 7-14,1.091; 57-63,1.057;	CAMP_PHOSPHO_SITE 280-283; PKC_PHOSPHO_SITE 65-67; CK2_PHOSPHO_SITE 36-39; MYRISTYL 2- 7; PKC_PHOSPHO_SITE 95-97; MYRISTYL 33-38; PKC_PHOSPHO_SITE 264-266; ASN_GLYCOSYLATION 248-251; PKC_PHOSPHO_SITE 144-146; CK2_PHOSPHO_SITE 209-212; PKC_PHOSPHO_SITE 250-252; MYRISTYL 53-58; CAMP_PHOSPHO_SITE 23-26; PKC_PHOSPHO_SITE 21-23;	
DEX0450- 044.aa.3	Y	3 - il- 6;tm7- 29;o30- 43;tm44- 63;i64- 101;tm102 - 121;o122- 301;		224-270,1.239; 101- 133,1.193; 170-176,1.037; 185-194,1.055; 293- 298,1.072; 93-98,1.057; 50- 70,1.293; 35-48,1.197; 207- 212,1.058; 277-290,1.265; 5-29,1.297;	CK2_PHOSPHO_SITE 142-145; PKC_PHOSPHO_SITE 197-199; PKC_PHOSPHO_SITE 77-79; CAMP_PHOSPHO_SITE 213-216; PKC_PHOSPHO_SITE 260-262; ASN_GLYCOSYLATION 181-184; PKC_PHOSPHO_SITE 28-30; CK2_PHOSPHO_SITE 278-281; PKC_PHOSPHO_SITE 183-185;	
DEX0450- 045.aa.1	N	0 - ol- 98;			PKC_PHOSPHO_SITE 20-22; CK2_PHOSPHO_SITE 25-28; CAMP_PHOSPHO_SITE 49-52; MYRISTYL 2-	NONHISHMGI7 57-71; NONHISHMGI7 85-95; NONHISHMGI7 72-84;

				7; MYRISTYL 16-21; CAMP_PHOSPHO_SITE 73-76; PKC_PHOSPHO_SITE 76-78; AMIDATION 38-41; PKC_PHOSPHO_SITE 68-70;	
DEX0450-045.orf.1	N	0 - ol-130;		PKC_PHOSPHO_SITE 73-75; PKC_PHOSPHO_SITE 80-82; MYRISTYL 124-129; PKC_PHOSPHO_SITE 11-13; MYRISTYL 51-56; CK2_PHOSPHO_SITE 101-104; PKC_PHOSPHO_SITE 40-42; PKC_PHOSPHO_SITE 125-127; PKC_PHOSPHO_SITE 59-61; PKC_PHOSPHO_SITE 86-88; CK2_PHOSPHO_SITE 125-128;	HISTAMINEH3R 5-20; PRICHEXTENSIN 3-15; PRO_RICH 3-84; PRICHEXTENSIN 26-47; HISTAMINEH3R 81-107; PRICHEXTENSIN 49-65; PRICHEXTENSIN 66-83;
DEX0450-046.aa.1	N	0 - ol-260;	247-253, 1.054; 23-48, 1.204; 75-83, 1.044; 239-244, 1.043; 219-226, 1.11; 149- 155, 1.064; 60-66, 1.121; 133-141, 1.104; 89-94, 1.029; 179-186, 1.105; 168- 173, 1.075; 105-121, 1.209; 123-130, 1.041;	PKC_PHOSPHO_SITE 132-134; MYRISTYL 105-110; ASN_GLYCOSYLATION 13-16; MYRISTYL 117-122; PKC_PHOSPHO_SITE 15-17; MYRISTYL 18-23; CK2_PHOSPHO_SITE 112-115; MYRISTYL 101-106; CK2_PHOSPHO_SITE 184-187; MYRISTYL 232-237; MYRISTYL 97-102; CK2_PHOSPHO_SITE 119-122; CK2_PHOSPHO_SITE 242-245; MYRISTYL 21-26; MYRISTYL 200-205; PKC_PHOSPHO_SITE 143-145;	RRM 107-184; rrm 109-179; RRM 108-180;
DEX0450-046.orf.1	N	0 - ol-243;		AMIDATION 44-47; CK2_PHOSPHO_SITE 54-57; MYRISTYL 34-39; MYRISTYL 185-190; PKC_PHOSPHO_SITE 201-203; AMIDATION 52-55; MYRISTYL 43-48; PKC_PHOSPHO_SITE 93-95; CK2_PHOSPHO_SITE 225-228; MYRISTYL 215-220; MYRISTYL 102-107; CK2_PHOSPHO_SITE 169-172; RGD 87-89; PKC_PHOSPHO_SITE 76-78; CK2_PHOSPHO_SITE 104-107; MYRISTYL 193-198; PKC_PHOSPHO_SITE 68-70; CK2_PHOSPHO_SITE 1-4; MYRISTYL 200-	rrm 94-164; RRM 92-169; RRM 93-165;

				205; MYRISTYL 30-35; MYRISTYL 196-201; PKC_PHOSPHO_SITE 117-119; MYRISTYL 39-44; CK2_PHOSPHO_SITE 44-47; MYRISTYL 38-43; PKC_PHOSPHO_SITE 44-46; PKC_PHOSPHO_SITE 128-130;	
DEX0450_047.aa.1	N	0 - 01-428;	300-316, 1.166; 158-176, 1.167; 178-201, 1.106; 246-252, 1.107; 351-363, 1.107; 324-337, 1.16; 389-397, 1.093; 371-383, 1.222; 23-29, 1.068; 120-155, 1.174; 203-209, 1.065; 268-277, 1.076; 284-297, 1.059; 399-415, 1.154; 227-237, 1.151; 81-99, 1.188; 212-223, 1.117;	PKC_PHOSPHO_SITE 282-284; PKC_PHOSPHO_SITE 355-357; MYRISTYL 236-241; PKC_PHOSPHO_SITE 23-25; CK2_PHOSPHO_SITE 318-321; PKC_PHOSPHO_SITE 56-58; CK2_PHOSPHO_SITE 109-112; PKC_PHOSPHO_SITE 318-320; MYRISTYL 98-103; PKC_PHOSPHO_SITE 10-12; PKC_PHOSPHO_SITE 120-122; CK2_PHOSPHO_SITE 30-33; MYRISTYL 232-237; CK2_PHOSPHO_SITE 113-116; CK2_PHOSPHO_SITE 2-5; PKC_PHOSPHO_SITE 252-254;	ENDOLAPTASE 231-247; ENDOLAPTASE 348-367; ENDOLAPTASE 371-389; FMOXYGENASE 90-106; ENDOLAPTASE 318-337; LON_SER 321-329; FMOXYGENASE 343-360;
DEX0450_047.orf.1	N	0 - 01-287;		PKC_PHOSPHO_SITE 5-7; PKC_PHOSPHO_SITE 177-179; ASN_GLYCOSYLATION 4-7; PKC_PHOSPHO_SITE 141-143; MYRISTYL 95-100; MYRISTYL 5-10; PKC_PHOSPHO_SITE 111-113; CK2_PHOSPHO_SITE 177-180; LEUCINE_ZIPPER 5-26; PKC_PHOSPHO_SITE 214-216; MYRISTYL 91-96;	TONB_DEPENDENT_REC 1 1-68; ENDOLAPTASE 177-196; ENDOLAPTASE 90-106; ENDOLAPTASE 230-248; LON_SER 180-188; ENDOLAPTASE 207-226;
DEX0450_048.aa.1	N	0 - 01-247;	36-42, 1.056; 92-106, 1.093; 16-34, 1.191; 220-226, 1.066; 120-130, 1.078; 133-140, 1.074; 161-183, 1.131; 228-244, 1.126; 64-81, 1.201; 4-9, 1.114; 148-153, 1.049;	ASN_GLYCOSYLATION 133-136; CK2_PHOSPHO_SITE 119-122; CK2_PHOSPHO_SITE 59-62; MYRISTYL 203-208; MYRISTYL 207-212; PKC_PHOSPHO_SITE 116-118;	TCOMPLEXTCP1 136-148; TCOMPLEXTCP1 102-124; cpn60_TCP1 1-245;
DEX0450_048.orf.	N	0 - 01-154;		ASN_GLYCOSYLATION 40-43; MYRISTYL 47-52; CK2_PHOSPHO_SITE 26-29;	TCOMPLEXTCP1 43-55; TCOMPLEXTCP1 9-31;

1					MYRISTYL 110-115; PKC_PHOSPHO_SITE 23-25; MYRISTYL 51-56; MYRISTYL 114-119;	
DEX0450-049.aa.1	N	0 - 01-269;			CK2_PHOSPHO_SITE 18-21; ASN_GLYCOSYLATION 27-30; TYR_PHOSPHO_SITE 58-65; CK2_PHOSPHO_SITE 236-239; MYRISTYL 57-62; CK2_PHOSPHO_SITE 60-63; PKC_PHOSPHO_SITE 25-27; CK2_PHOSPHO_SITE 76-79; PKC_PHOSPHO_SITE 98-100; CK2_PHOSPHO_SITE 94-97; AMIDATION 48-51; ASN_GLYCOSYLATION 58-61; MYRISTYL 215-220; CK2_PHOSPHO_SITE 68-71; CK2_PHOSPHO_SITE 99-102; AMIDATION 75-78; PKC_PHOSPHO_SITE 48-50; CK2_PHOSPHO_SITE 239-242; MYRISTYL 95-100; MYRISTYL 94-99; CK2_PHOSPHO_SITE 110-113; PKC_PHOSPHO_SITE 145-147; TYR_PHOSPHO_SITE 7-15; AMIDATION 124-127; PKC_PHOSPHO_SITE 53-55; MYRISTYL 229-234; ASN_GLYCOSYLATION 175-178; CK2_PHOSPHO_SITE 112-115; CK2_PHOSPHO_SITE 32-35; PKC_PHOSPHO_SITE 29-31; PKC_PHOSPHO_SITE 76-78; MYRISTYL 45-50; PKC_PHOSPHO_SITE 112-114; CAMP_PHOSPHO_SITE 50-53; CK2_PHOSPHO_SITE 146-149; TYR_PHOSPHO_SITE 127-135; CK2_PHOSPHO_SITE 29-32; ASN_GLYCOSYLATION 51-54; CK2_PHOSPHO_SITE 114-117;	sp_060568_PLO3_HUMAN 143-266;
DEX0450-049.orf.	N	0 - 01-138;			PKC_PHOSPHO_SITE 3-5; TYR_PHOSPHO_SITE 5-13;	sp_060568_PLO3_HUMAN 21-138;

1						PKC_PHOSPHO_SITE 23-25; CK2_PHOSPHO_SITE 24-27; ASN_GLYCOSYLATION 53-56; MYRISTYL 73-78; MYRISTYL 95-100;		
DEX0450_050.aa.1	Y	4 - i1- 25;tm26- 48;o49- 71;tm72- 94;i95- 100;tm101 - 123;o124- 154;tm155 - 177;i178- 233;	12-50,1.341; 189-197,1.212; 213-228,1.15; 114- 140,1.199; 146-182,1.264; 72-89,1.185; 99-112,1.16; 200-207,1.154;	ASN_GLYCOSYLATION 187-190; CK2_PHOSPHO_SITE 196-199; ASN_GLYCOSYLATION 54-57; TYR_PHOSPHO_SITE 186-194; PKC_PHOSPHO_SITE 230-232; CK2_PHOSPHO_SITE 56-59; PKC_PHOSPHO_SITE 167-169; ASN_GLYCOSYLATION 198-201; CK2_PHOSPHO_SITE 128-131; MYRISTYL 214-219;	Mtp 32-226;			
DEX0450_050.orf.1	N	4 - i1- 109;tm110 - 132;o133- 155;tm156 - 178;i179- 184;tm185 - 207;o208- 238;tm239 - 261;i262- 319;		PKC_PHOSPHO_SITE 14-16; PKC_PHOSPHO_SITE 58-60; MYRISTYL 43- 48; MYRISTYL 54-59; MYRISTYL 47-52; PKC_PHOSPHO_SITE 30-32; CK2_PHOSPHO_SITE 140-143; TYR_PHOSPHO_SITE 270-278; MYRISTYL 48-53; ASN_GLYCOSYLATION 138-141; MYRISTYL 298-303; CK2_PHOSPHO_SITE 280-283; CK2_PHOSPHO_SITE 12-15; ASN_GLYCOSYLATION 282-285; MYRISTYL 49-54; ASN_GLYCOSYLATION 271-274; MYRISTYL 61-66; CAMP_PHOSPHO_SITE 66-69; PKC_PHOSPHO_SITE 251-253; MYRISTYL 57-62; CK2_PHOSPHO_SITE 212-215; MYRISTYL 51-56;	Mtp 116-305;			
DEX0450_051.aa.1	N	0 - o1- 76;	8-18,1.155; 66-73,1.117; 23-61,1.206;	MYRISTYL 25-30; MYRISTYL 9-14; MYRISTYL 5-10; MYRISTYL 16-21;				
DEX0450_051.orf.1	Y	0 - o1- 72;	53-69,1.054; 4-14,1.166; 42-49,1.071; 27-37,1.155;	MYRISTYL 35-40; ASN_GLYCOSYLATION 52-55; MYRISTYL 24-29; CK2 PHOSPHO_SITE 18-21;	ANTIFREEZEI 52-61; ANTIFREEZEI 18-32;			

DEX0450-051.aa.2	N	0 - ol-61;	11-46,1.206; 51-58,1.117;	PKC_PHOSPHO_SITE 15-17; MYRISTYL 28-33; MYRISTYL 44-49;	
DEX0450-051.orf.2	N	0 - ol-57;	6-15,1.118; 19-42,1.206; 47-54,1.117;	CK2_PHOSPHO_SITE 13-16;	
DEX0450-052.aa.1	N	0 - ol-267;		CK2_PHOSPHO_SITE 5-8; PKC_PHOSPHO_SITE 5-7; PKC_PHOSPHO_SITE 149-151; CK2_PHOSPHO_SITE 144-147; PKC_PHOSPHO_SITE 160-162; ASN_GLYCOSYLATION 128-131; MYRISTYL 251-256; CK2_PHOSPHO_SITE 95-98; PKC_PHOSPHO_SITE 134-136; MYRISTYL 64-69; CK2_PHOSPHO_SITE 90-93; PKC_PHOSPHO_SITE 144-146; CAMP_PHOSPHO_SITE 150-153;	NAP 10-208;
DEX0450-052.orf.1	N	0 - ol-148;		ASN_GLYCOSYLATION 22-25; PKC_PHOSPHO_SITE 1-3; PKC_PHOSPHO_SITE 28-30; CK2_PHOSPHO_SITE 141-144; CK2_PHOSPHO_SITE 38-41; CAMP_PHOSPHO_SITE 44-47; PKC_PHOSPHO_SITE 43-45; PKC_PHOSPHO_SITE 54-56; PKC_PHOSPHO_SITE 38-40;	NAP 1-102;
DEX0450-053.aa.1	Y	4 - il-25;tm26-48;o49-79;tm80-102;i103-108;tm109-131;o132-162:tml63	226-231,1.116; 12-50,1.341; 208-215,1.154; 154-190,1.264; 107-120,1.116; 78-97,1.185; 197-205,1.212; 71-76,1.085; 122-148,1.199;	PKC_PHOSPHO_SITE 175-177; TYR_PHOSPHO_SITE 194-202; CK2_PHOSPHO_SITE 56-59; ASN_GLYCOSYLATION 195-198; ASN_GLYCOSYLATION 75-78; ASN_GLYCOSYLATION 206-209; ASN_GLYCOSYLATION 54-57; CK2_PHOSPHO_SITE 136-139; CK2_PHOSPHO_SITE 204-207;	Mtp 32-234;

Example 1b: Sequence Alignment Support

Alignments between previously identified sequences and splice variant sequences are performed to confirm unique portions of splice variant nucleic acid and amino acid sequences. The alignments are done using the Needle program in the European Molecular
5 Biology Open Software Suite (EMBOSS) version 2.2.0 available at www.emboss.org from EMBnet (<http://www.embnnet.org>). Default settings are used unless otherwise noted. The Needle program in EMBOSS implements the Needleman-Wunsch algorithm. Needleman, S. B., Wunsch, C. D., *J. Mol. Biol.* 48:443-453 (1970).

It is well know to those skilled in the art that implication of alignment algorithms
10 by various programs may result in minor changes in the generated output. These changes include but are not limited to: alignment scores (percent identity, similarity, and gap), display of nonaligned flanking sequence regions, and number assignment to residues. These minor changes in the output of an alignment do not alter the physical characteristics of the sequences or the differences between the sequences, e.g. regions of homology,
15 insertions, or deletions.

Example 1c: RT-PCR Analysis

To detect the presence and tissue distribution of a particular splice variant Reverse Transcription-Polymerase Chain Reaction (RT-PCR) is performed using cDNA generated from a panel of tissue RNAs. *See, e.g.,* Sambrook *et al.*, Molecular Cloning: A Laboratory
20 Manual, 2d ed., Cold Spring Harbor Laboratory Press (1989) and; Kawasaki ES *et al.*, *PNAS* 85(15):5698 (1988). Total RNA is extracted from a variety of tissues and first strand cDNA is prepared with reverse transcriptase (RT). Each panel includes 23 cDNAs from five cancer types (lung, ovary, breast, colon, and prostate) and normal samples of testis, placenta and fetal brain. Each cancer set is composed of three cancer cDNAs from
25 different donors and one normal pooled sample. Using a standard enzyme kit from BD Bioscience Clontech (Mountain View, CA), the target transcript is detected with sequence-specific primers designed to only amplify the particular splice variant. The PCR reaction is run on the GeneAmp PCR system 9700 (Applied Biosystem, Foster City, CA) thermocycler under optimal conditions. One of ordinary skill can design appropriate
30 primers and determine optimal conditions. The amplified product is resolved on an agarose gel to detect a band of equivalent size to the predicted RT-PCR product. A band

indicated the presence of the splice variant in a sample. The relation of the amplified product to the splice variant was subsequently confirmed by DNA sequencing.

After subcloning, all positively screened clones are sequence verified. The DNA sequence verification results show the splice variant contains the predicted sequence
5 differences in comparison with the reference sequence.

Results for RT-PCR analysis in the table below include the sequence DEX ID, Lead Name, Cancer Tissue(s) the transcript was detected in, Normal Tissue(s) the transcript was detected in, the predicted length of the RT-PCR product, and the Confirmed Length of the RT-PCR product.

DEX ID	Lead Name	Cancer Tissue(s)	Normal Tissue(s)	Predicted Length	Confirmed Length
DEX0450_007.nt.1	Cln260	Prostate	Ovary	365bp	365bp

10

RT-PCR results confirm the presence SEQ ID NO: 1-94 in biologic samples and distinguish between related transcripts.

Example 1d: Secretion Assay

To determine if a protein encoded by a splice variant is secreted from cells a
15 secretion assay is preformed. A pcDNA3.1 clone containing the gene transcript which encodes the variant protein is transfected into 293T cells using the Superfect transfection reagent (Qiagen, Valencia CA). Transfected cells are incubated for 28 hours before the media is collected and immediately spun down to remove any detached cells. The adherent cells are solubilized with lysis buffer (1% NP40, 10mM sodium phosphate
20 pH7.0, and 0.15M NaCl). The lysed cells are collected and spun down and the supernatant extracted as cell lysate. Western immunoblot is carried out in the following manner: 15µl of the cell lysate and media are run on 4-12% NuPage Bis-Tris gel (Invitrogen, Carlsbad CA), and blotted onto a PVDF membrane (Invitrogen, Carlsbad CA). The blot is incubated with a polyclonal primary antibody which binds to the variant
25 protein (Imgenex, San Diego CA) and polyclonal goat anti-rabbit-peroxidase secondary antibody (Sigma-Aldrich, St. Louis MO). The blot is developed with the ECL Plus chemiluminescent detection reagent (Amersham BioSciences, Piscataway NJ).

Secretion assay results are indicative of SEQ ID NO: 95-248 being a diagnostic marker and/or therapeutic target for cancer.

30 **Example 2a: Gene Expression Analysis**

Custom Microarray Experiment - Cancer

Custom oligonucleotide microarrays were provided by Agilent Technologies, Inc. (Palo Alto, CA). The microarrays were fabricated by Agilent using their technology for the *in-situ* synthesis of 60mer oligonucleotides (Hughes, et al. 2001, Nature Biotechnology 19:342-347). The 60mer microarray probes were designed by Agilent, from gene
5 sequences provided by diaDexus, using Agilent proprietary algorithms. Whenever possible two different 60mers were designed for each gene of interest.

All microarray experiments were two-color experiments and were performed using Agilent-recommended protocols and reagents. Briefly, each microarray was hybridized
10 with cRNAs synthesized from RNA (total RNA for ovarian and prostate, polyA+ RNA for lung, breast and colon samples), isolated from cancer and normal tissues, labeled with fluorescent dyes Cyanine3 (Cy3) or Cyanine5 (Cy5) (NEN Life Science Products, Inc., Boston, MA) using a linear amplification method (Agilent). In each experiment the experimental sample was RNA isolated from cancer tissue from a single individual and
15 the reference sample was a pool of RNA isolated from normal tissues of the same organ as the cancerous tissue (*i.e.* normal ovarian tissue in experiments with ovarian cancer samples). Hybridizations were carried out at 60°C, overnight using Agilent *in-situ* hybridization buffer. Following washing, arrays were scanned with a GenePix 4000B Microarray Scanner (Axon Instruments, Inc., Union City, CA). The resulting images were
20 analyzed with GenePix Pro 3.0 Microarray Acquisition and Analysis Software (Axon).

Data normalization and expression profiling were done with Expressionist software from GeneData Inc. (Daly City, CA/Basel, Switzerland). Gene expression analysis was performed using only experiments that met certain quality criteria. The quality criteria that experiments must meet are a combination of evaluations performed by
25 the Expressionist software and evaluations performed manually using raw and normalized data. To evaluate raw data quality, detection limits (the mean signal for a replicated negative control + 2 Standard Deviations (SD)) for each channel were calculated. The detection limit is a measure of non-specific hybridization. Acceptable detection limits were defined for each dye (<80 for Cy5 and <150 for Cy3). Arrays with poor detection
30 limits in one or both channels were not analyzed and the experiments were repeated. To evaluate normalized data quality, positive control elements included in the array were utilized. These array features should have a mean ratio of 1 (no differential expression). If these features have a mean ratio of greater than 1.5-fold up or down, the experiments

were not analyzed further and were repeated. In addition to traditional scatter plots demonstrating the distribution of signal in each experiment, the Expressionist software also has minimum thresholding criteria that employ user defined parameters to identify quality data. These thresholds include two distinct quality measurements: 1) minimum area percentage, which is a measure of the integrity of each spot and 2) signal to noise ratio, which ensures that the signal being measured is significantly above any background (nonspecific) signal present. Only those features that met the threshold criteria were included in the filtering and analyses carried out by Expressionist. The thresholding settings employed require a minimum area percentage of 60% [(% pixels > background + 2SD)-(% pixels saturated)], and a minimum signal to noise ratio of 2.0 in both channels. By these criteria, very low expressors, saturated features and spots with abnormally high local background were not included in analysis.

Relative expression data was collected from Expressionist based on filtering and clustering analyses. Up-regulated genes were identified using criteria for the percentage of experiments in which the gene is up-regulated by at least 2-fold. In general, up-regulation in ~30% of samples tested was used as a cutoff for filtering.

Two microarray experiments were performed for each normal and cancer tissue pair. The tissue specific Array Chip for each cancer tissue is a unique microarray specific to that tissue and cancer. The Multi-Cancer Array Chip is a universal microarray that was hybridized with samples from each of the cancers (ovarian, breast, colon, lung, and prostate). See the description below for the experiments specific to the different cancers.

Microarray Experiments and Data Tables

COLON CANCER CHIPS

For colon cancer two different chip designs were evaluated with overlapping sets of a total of 38 samples, comparing the expression patterns of colon cancer derived polyA+ RNA to polyA+ RNA isolated from a pool of 7 normal colon tissues. For the Colon Array Chip all 38 samples (23 Ascending colon carcinomas and 15 Rectosigmoidal carcinomas including: 5 stage I cancers, 15 stage II cancers, 15 stage III and 2 stage IV cancers, as well as 28 Grade 1/2 and 10 Grade 3 cancers) were analyzed. The histopathologic grades for cancer are classified as follows: GX, cannot be assessed; G1, well differentiated; G2, Moderately differentiated; G3, poorly differentiated; and G4, undifferentiated. AJCC Cancer Staging Handbook, 5th Edition, 1998, page 9. For the

Colon Array Chip analysis, samples were further divided into groups based on the expression pattern of the known colon cancer associated gene Thymidilate Synthase (TS) (13 TS up 25 TS not up). The association of TS with advanced colorectal cancer is well documented. Paradiso *et al.*, *Br J Cancer* 82(3):560-7 (2000); Etienne *et al.*, *J Clin Oncol.* 20(12):2832-43 (2002); Aschele *et al.* *Clin Cancer Res.* 6(12):4797-802 (2000).

For the Multi-Cancer Array Chip a subset of 27 of these samples (14 Ascending colon carcinomas and 13 Rectosigmoidal carcinomas including: 3 stage I cancers, 9 stage II cancers, 13 stage III and 2 stage IV cancers) were assessed.

The results for the statistically significant up-regulated genes on the Colon Array Chip are shown in Tables 1 and 2. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 3.

The first two columns of each table contain information about the sequence itself (Seq ID, Oligo Name), the next columns show the results obtained for all ("ALL") the colon samples, ascending colon carcinomas ("ASC"), Rectosigmoidal carcinomas ("RS"), cancers corresponding to stages I and II ("ST1,2"), stages III and IV ("ST3,4"), grades 1 and 2 ("GR1,2"), grade 3 ("GR3"), cancers exhibiting up-regulation of the TS gene ("TSup") or those not exhibiting up-regulation of the TS gene ("NOT TSup"). '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed n=38 for the Colon Array Chip (n=27 for the Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

Table 1.

DEX ID	Oligo Name	Cln ALL %up n=38	Cln ALL %val id up n=38	Cln ASC %up n=23	Cln ASC %valid up n=23	Cln RS %up n=15	Cln RS % valid up n=15	Cln ST1,2 %up n=20	Cln ST1,2 % valid up n=20	Cln ST3,4 %up n=18	Cln ST3,4 %vali d up n=18
DEX0450_002.nt.1	31003.0	5.3	5.9	4.3	4.8	6.7	7.7	0.0	0.0	11.1	11.8
DEX0450_002.nt.1	31158.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_002.nt.1	31159.0	10.5	10.5	13.0	13.0	6.7	6.7	5.0	5.0	16.7	16.7
DEX0450_002.nt.1	31162.0	15.8	16.2	26.1	26.1	0.0	0.0	15.0	15.8	16.7	16.7
DEX0450_002.nt.1	31163.0	7.9	7.9	13.0	13.0	0.0	0.0	5.0	5.0	11.1	11.1
DEX0450_002.nt.1	34074.0	13.2	14.7	17.4	19.0	6.7	7.7	5.0	5.9	22.2	23.5

DEX0450_002. nt.1	34075.0	2.6	2.7	0.0	0.0	6.7	6.7	0.0	0.0	5.6	5.9
DEX0450_003. nt.1	31446.0	2.6	3.1	0.0	0.0	6.7	7.1	0.0	0.0	5.6	6.7
DEX0450_003. nt.2	31447.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_003. nt.3	31443.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_003. nt.3	31447.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_004. nt.1	10720.0	36.8	36.8	21.7	21.7	60.0	60.0	30.0	30.0	44.4	44.4
DEX0450_004. nt.1	10721.0	36.8	36.8	21.7	21.7	60.0	60.0	30.0	30.0	44.4	44.4
DEX0450_005. nt.1	16776.0	2.6	3.1	4.3	5.0	0.0	0.0	0.0	0.0	5.6	7.1
DEX0450_005. nt.1	16777.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_005. nt.1	38049.0	47.4	47.4	43.5	43.5	53.3	53.3	50.0	50.0	44.4	44.4
DEX0450_005. nt.1	38050.0	55.3	55.3	47.8	47.8	66.7	66.7	60.0	60.0	50.0	50.0
DEX0450_006. nt.1	35170.0	28.9	84.6	21.7	71.4	40.0	100.0	30.0	85.7	27.8	83.3
DEX0450_006. nt.1	35171.0	21.1	40.0	21.7	35.7	20.0	50.0	25.0	45.5	16.7	33.3
DEX0450_007. nt.1	35170.0	28.9	84.6	21.7	71.4	40.0	100.0	30.0	85.7	27.8	83.3
DEX0450_007. nt.1	35171.0	21.1	40.0	21.7	35.7	20.0	50.0	25.0	45.5	16.7	33.3
DEX0450_008. nt.1	30227.0	50.0	50.0	60.9	60.9	33.3	33.3	55.0	55.0	44.4	44.4
DEX0450_008. nt.1	30228.0	44.7	44.7	56.5	56.5	26.7	26.7	45.0	45.0	44.4	44.4
DEX0450_009. nt.1	39839.0	10.5	10.5	13.0	13.0	6.7	6.7	0.0	0.0	22.2	22.2
DEX0450_009. nt.1	39840.0	10.5	10.8	13.0	13.6	6.7	6.7	0.0	0.0	22.2	22.2
DEX0450_009. nt.2	39839.0	10.5	10.5	13.0	13.0	6.7	6.7	0.0	0.0	22.2	22.2
DEX0450_009. nt.2	39840.0	10.5	10.8	13.0	13.6	6.7	6.7	0.0	0.0	22.2	22.2
DEX0450_010. nt.1	29571.0	31.6	31.6	43.5	43.5	13.3	13.3	25.0	25.0	38.9	38.9
DEX0450_010. nt.1	29582.0	52.6	52.6	60.9	60.9	40.0	40.0	45.0	45.0	61.1	61.1
DEX0450_010. nt.1	29595.0	52.6	52.6	56.5	56.5	46.7	46.7	45.0	45.0	61.1	61.1
DEX0450_010. nt.1	29609.0	47.4	47.4	52.2	52.2	40.0	40.0	40.0	40.0	55.6	55.6
DEX0450_010. nt.1	29611.0	52.6	52.6	56.5	56.5	46.7	46.7	45.0	45.0	61.1	61.1
DEX0450_010. nt.1	29612.0	50.0	50.0	52.2	52.2	46.7	46.7	45.0	45.0	55.6	55.6
DEX0450_010. nt.2	29582.0	52.6	52.6	60.9	60.9	40.0	40.0	45.0	45.0	61.1	61.1
DEX0450_010. nt.2	29595.0	52.6	52.6	56.5	56.5	46.7	46.7	45.0	45.0	61.1	61.1

DEX0450_010. nt.2	29609.0	47.4	47.4	52.2	52.2	40.0	40.0	40.0	40.0	55.6	55.6
DEX0450_010. nt.2	29611.0	52.6	52.6	56.5	56.5	46.7	46.7	45.0	45.0	61.1	61.1
DEX0450_010. nt.2	29612.0	50.0	50.0	52.2	52.2	46.7	46.7	45.0	45.0	55.6	55.6
DEX0450_010. nt.3	29571.0	31.6	31.6	43.5	43.5	13.3	13.3	25.0	25.0	38.9	38.9
DEX0450_010. nt.3	29572.0	5.3	5.3	4.3	4.3	6.7	6.7	10.0	10.0	0.0	0.0
DEX0450_010. nt.3	29582.0	52.6	52.6	60.9	60.9	40.0	40.0	45.0	45.0	61.1	61.1
DEX0450_010. nt.3	29595.0	52.6	52.6	56.5	56.5	46.7	46.7	45.0	45.0	61.1	61.1
DEX0450_010. nt.3	29609.0	47.4	47.4	52.2	52.2	40.0	40.0	40.0	40.0	55.6	55.6
DEX0450_010. nt.3	29611.0	52.6	52.6	56.5	56.5	46.7	46.7	45.0	45.0	61.1	61.1
DEX0450_010. nt.3	29612.0	50.0	50.0	52.2	52.2	46.7	46.7	45.0	45.0	55.6	55.6
DEX0450_010. nt.3	36747.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_011. nt.1	22654.0	10.5	10.5	17.4	17.4	0.0	0.0	10.0	10.0	11.1	11.1
DEX0450_012. nt.1	8377.0	13.2	13.2	21.7	21.7	0.0	0.0	15.0	15.0	11.1	11.1
DEX0450_013. nt.1	32220.0	47.4	47.4	43.5	43.5	53.3	53.3	30.0	30.0	66.7	66.7
DEX0450_013. nt.1	32221.0	60.5	63.9	52.2	54.5	73.3	78.6	50.0	52.6	72.2	76.5
DEX0450_013. nt.1	32254.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_013. nt.1	32255.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_013. nt.1	33033.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_014. nt.1	32458.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_014. nt.1	32459.0	5.3	5.4	8.7	8.7	0.0	0.0	0.0	0.0	11.1	11.1
DEX0450_015. nt.1	33503.0	18.4	18.9	30.4	31.8	0.0	0.0	15.0	15.8	22.2	22.2
DEX0450_016. nt.1	33083.0	5.3	5.3	4.3	4.3	6.7	6.7	10.0	10.0	0.0	0.0
DEX0450_016. nt.1	35091.0	21.1	21.1	30.4	30.4	6.7	6.7	20.0	20.0	22.2	22.2
DEX0450_016. nt.2	33083.0	5.3	5.3	4.3	4.3	6.7	6.7	10.0	10.0	0.0	0.0
DEX0450_016. nt.2	35091.0	21.1	21.1	30.4	30.4	6.7	6.7	20.0	20.0	22.2	22.2
DEX0450_016. nt.3	33083.0	5.3	5.3	4.3	4.3	6.7	6.7	10.0	10.0	0.0	0.0
DEX0450_016. nt.3	35091.0	21.1	21.1	30.4	30.4	6.7	6.7	20.0	20.0	22.2	22.2
DEX0450_017. nt.1	36711.0	2.6	2.6	0.0	0.0	6.7	6.7	0.0	0.0	5.6	5.6
DEX0450_017. nt.1	36712.0	2.6	2.8	0.0	0.0	6.7	7.1	0.0	0.0	5.6	5.9

DEX0450_017. nt.1	39631.0	2.6	2.8	0.0	0.0	6.7	7.1	0.0	0.0	5.6	5.9
DEX0450_017. nt.1	39635.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_017. nt.1	39636.0	2.6	2.6	0.0	0.0	6.7	6.7	0.0	0.0	5.6	5.6
DEX0450_017. nt.1	39769.0	13.2	13.2	17.4	17.4	6.7	6.7	5.0	5.0	22.2	22.2
DEX0450_017. nt.1	39770.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_017. nt.2	36711.0	2.6	2.6	0.0	0.0	6.7	6.7	0.0	0.0	5.6	5.6
DEX0450_017. nt.2	39631.0	2.6	2.8	0.0	0.0	6.7	7.1	0.0	0.0	5.6	5.9
DEX0450_017. nt.2	39635.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_017. nt.2	39636.0	2.6	2.6	0.0	0.0	6.7	6.7	0.0	0.0	5.6	5.6
DEX0450_017. nt.2	39769.0	13.2	13.2	17.4	17.4	6.7	6.7	5.0	5.0	22.2	22.2
DEX0450_017. nt.2	39770.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_017. nt.3	39631.0	2.6	2.8	0.0	0.0	6.7	7.1	0.0	0.0	5.6	5.9
DEX0450_017. nt.3	39635.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_017. nt.3	39636.0	2.6	2.6	0.0	0.0	6.7	6.7	0.0	0.0	5.6	5.6
DEX0450_017. nt.3	39769.0	13.2	13.2	17.4	17.4	6.7	6.7	5.0	5.0	22.2	22.2
DEX0450_018. nt.1	31424.0	10.5	11.8	13.0	13.6	6.7	8.3	10.0	11.1	11.1	12.5
DEX0450_018. nt.1	31425.0	10.5	12.1	13.0	14.3	6.7	8.3	5.0	5.3	16.7	21.4
DEX0450_018. nt.2	31424.0	10.5	11.8	13.0	13.6	6.7	8.3	10.0	11.1	11.1	12.5
DEX0450_018. nt.2	31425.0	10.5	12.1	13.0	14.3	6.7	8.3	5.0	5.3	16.7	21.4
DEX0450_018. nt.3	31424.0	10.5	11.8	13.0	13.6	6.7	8.3	10.0	11.1	11.1	12.5
DEX0450_018. nt.3	31425.0	10.5	12.1	13.0	14.3	6.7	8.3	5.0	5.3	16.7	21.4
DEX0450_019. nt.1	32748.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_019. nt.1	33066.0	10.5	10.5	17.4	17.4	0.0	0.0	20.0	20.0	0.0	0.0
DEX0450_019. nt.1	33067.0	15.8	15.8	26.1	26.1	0.0	0.0	20.0	20.0	11.1	11.1
DEX0450_019. nt.1	35570.0	15.8	16.2	26.1	26.1	0.0	0.0	20.0	21.1	11.1	11.1
DEX0450_019. nt.1	35571.0	18.4	18.4	30.4	30.4	0.0	0.0	25.0	25.0	11.1	11.1
DEX0450_019. nt.2	32748.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_019. nt.2	33066.0	10.5	10.5	17.4	17.4	0.0	0.0	20.0	20.0	0.0	0.0
DEX0450_019. nt.2	33067.0	15.8	15.8	26.1	26.1	0.0	0.0	20.0	20.0	11.1	11.1

DEX0450_019. nt.2	35570.0	15.8	16.2	26.1	26.1	0.0	0.0	20.0	21.1	11.1	11.1
DEX0450_019. nt.2	35571.0	18.4	18.4	30.4	30.4	0.0	0.0	25.0	25.0	11.1	11.1
DEX0450_019. nt.3	32748.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_019. nt.3	33066.0	10.5	10.5	17.4	17.4	0.0	0.0	20.0	20.0	0.0	0.0
DEX0450_019. nt.3	33067.0	15.8	15.8	26.1	26.1	0.0	0.0	20.0	20.0	11.1	11.1
DEX0450_019. nt.3	35570.0	15.8	16.2	26.1	26.1	0.0	0.0	20.0	21.1	11.1	11.1
DEX0450_019. nt.3	35571.0	18.4	18.4	30.4	30.4	0.0	0.0	25.0	25.0	11.1	11.1
DEX0450_020. nt.1	32972.0	7.9	7.9	8.7	8.7	6.7	6.7	0.0	0.0	16.7	16.7
DEX0450_020. nt.1	32990.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.1	32991.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.1	32992.0	7.9	7.9	4.3	4.3	13.3	13.3	0.0	0.0	16.7	16.7
DEX0450_020. nt.1	32994.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.1	32995.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.1	35546.0	7.9	7.9	4.3	4.3	13.3	13.3	0.0	0.0	16.7	16.7
DEX0450_020. nt.2	32972.0	7.9	7.9	8.7	8.7	6.7	6.7	0.0	0.0	16.7	16.7
DEX0450_020. nt.2	32990.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.2	32991.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.2	32992.0	7.9	7.9	4.3	4.3	13.3	13.3	0.0	0.0	16.7	16.7
DEX0450_020. nt.2	32995.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.2	35546.0	7.9	7.9	4.3	4.3	13.3	13.3	0.0	0.0	16.7	16.7
DEX0450_020. nt.3	32972.0	7.9	7.9	8.7	8.7	6.7	6.7	0.0	0.0	16.7	16.7
DEX0450_020. nt.3	32990.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.3	32991.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.3	32992.0	7.9	7.9	4.3	4.3	13.3	13.3	0.0	0.0	16.7	16.7
DEX0450_020. nt.3	32995.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_020. nt.3	35546.0	7.9	7.9	4.3	4.3	13.3	13.3	0.0	0.0	16.7	16.7
DEX0450_021. nt.1	10700.0	2.6	4.5	4.3	6.7	0.0	0.0	5.0	7.7	0.0	0.0
DEX0450_021. nt.1	10701.0	2.6	3.4	0.0	0.0	6.7	10.0	0.0	0.0	5.6	7.1
DEX0450_021. nt.1	10744.0	15.8	17.1	17.4	19.0	13.3	14.3	15.0	16.7	16.7	17.6

DEX0450_021. nt.1	10745.0	5.3	6.5	8.7	10.5	0.0	0.0	0.0	0.0	11.1	12.5
DEX0450_022. nt.1	12057.0	10.5	11.1	13.0	14.3	6.7	6.7	5.0	5.3	16.7	17.6
DEX0450_022. nt.1	12058.0	2.6	2.6	0.0	0.0	6.7	6.7	0.0	0.0	5.6	5.6
DEX0450_023. nt.1	8910.0	26.3	26.3	34.8	34.8	13.3	13.3	25.0	25.0	27.8	27.8
DEX0450_024. nt.1	36564.0	34.2	34.2	39.1	39.1	26.7	26.7	30.0	30.0	38.9	38.9
DEX0450_025. nt.1	37705.0	26.3	26.3	21.7	21.7	33.3	33.3	30.0	30.0	22.2	22.2
DEX0450_025. nt.1	37706.0	21.1	21.1	13.0	13.0	33.3	33.3	20.0	20.0	22.2	22.2
DEX0450_027. nt.1	35470.0	34.2	34.2	39.1	39.1	26.7	26.7	30.0	30.0	38.9	38.9
DEX0450_027. nt.1	35471.0	42.1	42.1	43.5	43.5	40.0	40.0	35.0	35.0	50.0	50.0
DEX0450_027. nt.2	35470.0	34.2	34.2	39.1	39.1	26.7	26.7	30.0	30.0	38.9	38.9
DEX0450_027. nt.2	35471.0	42.1	42.1	43.5	43.5	40.0	40.0	35.0	35.0	50.0	50.0
DEX0450_028. nt.1	31539.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_028. nt.1	31545.0	13.2	13.2	17.4	17.4	6.7	6.7	10.0	10.0	16.7	16.7
DEX0450_030. nt.1	8410.0	13.2	13.2	13.0	13.0	13.3	13.3	15.0	15.0	11.1	11.1
DEX0450_030. nt.1	8411.0	13.2	13.2	13.0	13.0	13.3	13.3	15.0	15.0	11.1	11.1
DEX0450_031. nt.1	21356.0	18.4	18.9	30.4	31.8	0.0	0.0	20.0	21.1	16.7	16.7
DEX0450_031. nt.1	28423.0	18.4	18.9	30.4	30.4	0.0	0.0	20.0	20.0	16.7	17.6
DEX0450_031. nt.2	21356.0	18.4	18.9	30.4	31.8	0.0	0.0	20.0	21.1	16.7	16.7
DEX0450_032. nt.1	34888.0	18.4	18.4	26.1	26.1	6.7	6.7	20.0	20.0	16.7	16.7
DEX0450_033. nt.1	30532.0	44.7	44.7	60.9	60.9	20.0	20.0	50.0	50.0	38.9	38.9
DEX0450_033. nt.2	34642.0	23.7	30.0	30.4	43.8	13.3	14.3	25.0	31.2	22.2	28.6
DEX0450_033. nt.2	34643.0	21.1	24.2	30.4	36.8	6.7	7.1	20.0	22.2	22.2	26.7
DEX0450_034. nt.1	37498.0	7.9	7.9	8.7	8.7	6.7	6.7	5.0	5.0	11.1	11.1
DEX0450_035. nt.1	20153.0	21.1	21.6	21.7	22.7	20.0	20.0	20.0	21.1	22.2	22.2
DEX0450_035. nt.1	20154.0	7.9	7.9	4.3	4.3	13.3	13.3	15.0	15.0	0.0	0.0
DEX0450_036. nt.1	37615.0	47.4	47.4	39.1	39.1	60.0	60.0	50.0	50.0	44.4	44.4
DEX0450_036. nt.1	37616.0	44.7	44.7	34.8	34.8	60.0	60.0	45.0	45.0	44.4	44.4
DEX0450_036. nt.1	37635.0	42.1	42.1	34.8	34.8	53.3	53.3	45.0	45.0	38.9	38.9
DEX0450_037. nt.1	33741.0	44.7	47.2	39.1	42.9	53.3	53.3	50.0	50.0	38.9	43.8

DEX0450_038. nt.1	38975.0	15.8	15.8	21.7	21.7	6.7	6.7	15.0	15.0	16.7	16.7
DEX0450_038. nt.1	38976.0	18.4	18.4	17.4	17.4	20.0	20.0	15.0	15.0	22.2	22.2
DEX0450_039. nt.1	38501.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.1	38502.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.2	36599.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0450_039. nt.2	38428.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_039. nt.2	38499.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_039. nt.2	38501.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.2	38502.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.2	38509.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_039. nt.2	38510.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0450_039. nt.3	36599.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0450_039. nt.3	38428.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_039. nt.3	38499.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_039. nt.3	38501.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.3	38509.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_039. nt.3	38510.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0450_039. nt.4	36599.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0450_039. nt.4	38428.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_039. nt.4	38499.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_039. nt.4	38501.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.4	38502.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.4	38509.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0450_039. nt.4	38510.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0450_039. nt.5	38501.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.5	38502.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.6	38501.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_039. nt.6	38502.0	5.3	5.3	4.3	4.3	6.7	6.7	5.0	5.0	5.6	5.6
DEX0450_040. nt.1	35520.0	39.5	39.5	30.4	30.4	53.3	53.3	40.0	40.0	38.9	38.9

DEX0450_040. nt.1	35521.0	42.1	42.1	34.8	34.8	53.3	53.3	40.0	40.0	44.4	44.4
DEX0450_040. nt.1	39581.0	34.2	36.1	34.8	36.4	33.3	35.7	30.0	33.3	38.9	38.9
DEX0450_040. nt.1	39582.0	42.1	42.1	34.8	34.8	53.3	53.3	40.0	40.0	44.4	44.4
DEX0450_041. nt.1	33072.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0450_041. nt.1	33074.0	18.4	18.9	26.1	26.1	6.7	7.1	10.0	10.0	27.8	29.4
DEX0450_041. nt.1	33075.0	13.2	13.2	17.4	17.4	6.7	6.7	10.0	10.0	16.7	16.7
DEX0450_041. nt.1	36755.0	5.3	5.9	4.3	4.5	6.7	8.3	0.0	0.0	11.1	13.3
DEX0450_041. nt.1	36756.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_041. nt.1	37290.0	5.3	5.3	8.7	8.7	0.0	0.0	5.0	5.0	5.6	5.6
DEX0450_042. nt.1	33118.0	7.9	7.9	13.0	13.0	0.0	0.0	10.0	10.0	5.6	5.6
DEX0450_042. nt.1	33119.0	5.3	5.3	8.7	8.7	0.0	0.0	5.0	5.0	5.6	5.6
DEX0450_042. nt.1	34009.0	26.3	27.0	26.1	27.3	26.7	26.7	25.0	25.0	27.8	29.4
DEX0450_042. nt.1	40737.0	13.2	13.2	21.7	21.7	0.0	0.0	10.0	10.0	16.7	16.7
DEX0450_042. nt.2	33118.0	7.9	7.9	13.0	13.0	0.0	0.0	10.0	10.0	5.6	5.6
DEX0450_042. nt.2	33119.0	5.3	5.3	8.7	8.7	0.0	0.0	5.0	5.0	5.6	5.6
DEX0450_042. nt.2	34009.0	26.3	27.0	26.1	27.3	26.7	26.7	25.0	25.0	27.8	29.4
DEX0450_042. nt.2	40737.0	13.2	13.2	21.7	21.7	0.0	0.0	10.0	10.0	16.7	16.7
DEX0450_043. nt.1	35881.0	2.6	3.0	0.0	0.0	6.7	7.1	0.0	0.0	5.6	6.2
DEX0450_043. nt.1	35882.0	2.6	14.3	4.3	20.0	0.0	0.0	5.0	25.0	0.0	0.0
DEX0450_043. nt.1	36669.0	28.9	28.9	30.4	30.4	26.7	26.7	25.0	25.0	33.3	33.3
DEX0450_043. nt.1	36670.0	28.9	28.9	30.4	30.4	26.7	26.7	25.0	25.0	33.3	33.3
DEX0450_044. nt.1	9110.0	28.9	28.9	30.4	30.4	26.7	26.7	30.0	30.0	27.8	27.8
DEX0450_045. nt.1	13783.0	15.8	15.8	21.7	21.7	6.7	6.7	20.0	20.0	11.1	11.1
DEX0450_045. nt.1	13784.0	13.2	13.2	17.4	17.4	6.7	6.7	15.0	15.0	11.1	11.1
DEX0450_046. nt.1	10297.0	63.2	63.2	73.9	73.9	46.7	46.7	65.0	65.0	61.1	61.1
DEX0450_047. nt.1	30511.0	23.7	24.3	30.4	31.8	13.3	13.3	20.0	21.1	27.8	27.8
DEX0450_047. nt.1	38789.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_047. nt.1	39412.0	7.9	7.9	4.3	4.3	13.3	13.3	5.0	5.0	11.1	11.1
DEX0450_048. nt.1	41177.0	7.9	7.9	13.0	13.0	0.0	0.0	5.0	5.0	11.1	11.1

DEX0450_048. nt.1	41178.0	10.5	10.8	17.4	17.4	0.0	0.0	10.0	10.0	11.1	11.8
DEX0450_049. nt.1	31424.0	10.5	11.8	13.0	13.6	6.7	8.3	10.0	11.1	11.1	12.5
DEX0450_049. nt.1	31425.0	10.5	12.1	13.0	14.3	6.7	8.3	5.0	5.3	16.7	21.4
DEX0450_050. nt.1	9398.0	26.3	26.3	30.4	30.4	20.0	20.0	30.0	30.0	22.2	22.2
DEX0450_050. nt.1	9399.0	26.3	26.3	30.4	30.4	20.0	20.0	30.0	30.0	22.2	22.2
DEX0450_052. nt.1	37943.0	52.6	52.6	56.5	56.5	46.7	46.7	50.0	50.0	55.6	55.6
DEX0450_052. nt.1	37944.0	50.0	51.4	56.5	56.5	40.0	42.9	50.0	52.6	50.0	50.0
DEX0450_053. nt.1	9398.0	26.3	26.3	30.4	30.4	20.0	20.0	30.0	30.0	22.2	22.2
DEX0450_053. nt.1	9399.0	26.3	26.3	30.4	30.4	20.0	20.0	30.0	30.0	22.2	22.2

Table 2.

DEX ID	Oligo Name	Cln GR1,2 %up n=28	Cln GR1,2 %valid up n=28	Cln GR3 %up n=10	Cln GR3 %valid up n=10	Cln TS up %up n=13	Cln TS up %valid up n=13	Cln NOT TS up %up n=25	Cln NOT TS up %valid up n=25
DEX0450_002.nt.1	31003.0	0.0	0.0	20.0	22.2	15.4	15.4	0.0	0.0
DEX0450_002.nt.1	31158.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_002.nt.1	31159.0	0.0	0.0	40.0	40.0	23.1	23.1	4.0	4.0
DEX0450_002.nt.1	31162.0	14.3	14.8	20.0	20.0	23.1	23.1	12.0	12.5
DEX0450_002.nt.1	31163.0	3.6	3.6	20.0	20.0	15.4	15.4	4.0	4.0
DEX0450_002.nt.1	34074.0	3.6	4.0	40.0	44.4	30.8	33.3	4.0	4.5
DEX0450_002.nt.1	34075.0	0.0	0.0	10.0	11.1	7.7	7.7	0.0	0.0
DEX0450_003.nt.1	31446.0	0.0	0.0	10.0	14.3	7.7	11.1	0.0	0.0
DEX0450_003.nt.2	31447.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_003.nt.3	31443.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_003.nt.3	31447.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_004.nt.1	10720.0	42.9	42.9	20.0	20.0	7.7	7.7	52.0	52.0
DEX0450_004.nt.1	10721.0	46.4	46.4	10.0	10.0	15.4	15.4	48.0	48.0
DEX0450_005.nt.1	16776.0	3.6	4.0	0.0	0.0	7.7	8.3	0.0	0.0
DEX0450_005.nt.1	16777.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_005.nt.1	38049.0	50.0	50.0	40.0	40.0	61.5	61.5	40.0	40.0
DEX0450_005.nt.1	38050.0	60.7	60.7	40.0	40.0	61.5	61.5	52.0	52.0
DEX0450_006.nt.1	35170.0	35.7	83.3	10.0	100.0	7.7	33.3	40.0	100.0
DEX0450_006.nt.1	35171.0	28.6	47.1	0.0	0.0	7.7	16.7	28.0	50.0
DEX0450_007.nt.1	35170.0	35.7	83.3	10.0	100.0	7.7	33.3	40.0	100.0
DEX0450_007.nt.1	35171.0	28.6	47.1	0.0	0.0	7.7	16.7	28.0	50.0
DEX0450_008.nt.1	30227.0	42.9	42.9	70.0	70.0	61.5	61.5	44.0	44.0
DEX0450_008.nt.1	30228.0	35.7	35.7	70.0	70.0	53.8	53.8	40.0	40.0
DEX0450_009.nt.1	39839.0	3.6	3.6	30.0	30.0	23.1	23.1	4.0	4.0
DEX0450_009.nt.1	39840.0	3.6	3.7	30.0	30.0	23.1	23.1	4.0	4.2
DEX0450_009.nt.2	39839.0	3.6	3.6	30.0	30.0	23.1	23.1	4.0	4.0
DEX0450_009.nt.2	39840.0	3.6	3.7	30.0	30.0	23.1	23.1	4.0	4.2
DEX0450_010.nt.1	29571.0	28.6	28.6	40.0	40.0	46.2	46.2	24.0	24.0
DEX0450_010.nt.1	29582.0	46.4	46.4	70.0	70.0	61.5	61.5	48.0	48.0
DEX0450_010.nt.1	29595.0	50.0	50.0	60.0	60.0	69.2	69.2	44.0	44.0
DEX0450_010.nt.1	29609.0	46.4	46.4	50.0	50.0	61.5	61.5	40.0	40.0

DEX0450	010.nt.1	29611.0	50.0	50.0	60.0	60.0	69.2	69.2	44.0	44.0
DEX0450	010.nt.1	29612.0	50.0	50.0	50.0	50.0	69.2	69.2	40.0	40.0
DEX0450	010.nt.2	29582.0	46.4	46.4	70.0	70.0	61.5	61.5	48.0	48.0
DEX0450	010.nt.2	29595.0	50.0	50.0	60.0	60.0	69.2	69.2	44.0	44.0
DEX0450	010.nt.2	29609.0	46.4	46.4	50.0	50.0	61.5	61.5	40.0	40.0
DEX0450	010.nt.2	29611.0	50.0	50.0	60.0	60.0	69.2	69.2	44.0	44.0
DEX0450	010.nt.2	29612.0	50.0	50.0	50.0	50.0	69.2	69.2	40.0	40.0
DEX0450	010.nt.3	29571.0	28.6	28.6	40.0	40.0	46.2	46.2	24.0	24.0
DEX0450	010.nt.3	29572.0	7.1	7.1	0.0	0.0	7.7	7.7	4.0	4.0
DEX0450	010.nt.3	29582.0	46.4	46.4	70.0	70.0	61.5	61.5	48.0	48.0
DEX0450	010.nt.3	29595.0	50.0	50.0	60.0	60.0	69.2	69.2	44.0	44.0
DEX0450	010.nt.3	29609.0	46.4	46.4	50.0	50.0	61.5	61.5	40.0	40.0
DEX0450	010.nt.3	29611.0	50.0	50.0	60.0	60.0	69.2	69.2	44.0	44.0
DEX0450	010.nt.3	29612.0	50.0	50.0	50.0	50.0	69.2	69.2	40.0	40.0
DEX0450	010.nt.3	36747.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450	011.nt.1	22654.0	3.6	3.6	30.0	30.0	15.4	15.4	8.0	8.0
DEX0450	012.nt.1	8377.0	10.7	10.7	20.0	20.0	30.8	30.8	4.0	4.0
DEX0450	013.nt.1	32220.0	42.9	42.9	60.0	60.0	53.8	53.8	44.0	44.0
DEX0450	013.nt.1	32221.0	57.1	59.3	70.0	77.8	84.6	84.6	48.0	52.2
DEX0450	013.nt.1	32254.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450	013.nt.1	32255.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450	013.nt.1	33033.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450	014.nt.1	32458.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450	014.nt.1	32459.0	3.6	3.7	10.0	10.0	7.7	7.7	4.0	4.2
DEX0450	015.nt.1	33503.0	14.3	14.8	30.0	30.0	38.5	38.5	8.0	8.3
DEX0450	016.nt.1	33083.0	7.1	7.1	0.0	0.0	0.0	0.0	8.0	8.0
DEX0450	016.nt.1	35091.0	28.6	28.6	0.0	0.0	38.5	38.5	12.0	12.0
DEX0450	016.nt.2	33083.0	7.1	7.1	0.0	0.0	0.0	0.0	8.0	8.0
DEX0450	016.nt.2	35091.0	28.6	28.6	0.0	0.0	38.5	38.5	12.0	12.0
DEX0450	016.nt.3	33083.0	7.1	7.1	0.0	0.0	0.0	0.0	8.0	8.0
DEX0450	016.nt.3	35091.0	28.6	28.6	0.0	0.0	38.5	38.5	12.0	12.0
DEX0450	017.nt.1	36711.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.1	36712.0	0.0	0.0	10.0	10.0	7.7	8.3	0.0	0.0
DEX0450	017.nt.1	39631.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.1	39635.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450	017.nt.1	39636.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.1	39769.0	7.1	7.1	30.0	30.0	23.1	23.1	8.0	8.0
DEX0450	017.nt.1	39770.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450	017.nt.2	36711.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.2	39631.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.2	39635.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450	017.nt.2	39636.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.2	39769.0	7.1	7.1	30.0	30.0	23.1	23.1	8.0	8.0
DEX0450	017.nt.2	39770.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450	017.nt.3	39631.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.3	39635.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450	017.nt.3	39636.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450	017.nt.3	39769.0	7.1	7.1	30.0	30.0	23.1	23.1	8.0	8.0
DEX0450	018.nt.1	31424.0	7.1	8.0	20.0	22.2	23.1	23.1	4.0	4.8
DEX0450	018.nt.1	31425.0	3.6	4.0	30.0	37.5	30.8	30.8	0.0	0.0
DEX0450	018.nt.2	31424.0	7.1	8.0	20.0	22.2	23.1	23.1	4.0	4.8
DEX0450	018.nt.2	31425.0	3.6	4.0	30.0	37.5	30.8	30.8	0.0	0.0
DEX0450	018.nt.3	31424.0	7.1	8.0	20.0	22.2	23.1	23.1	4.0	4.8
DEX0450	018.nt.3	31425.0	3.6	4.0	30.0	37.5	30.8	30.8	0.0	0.0
DEX0450	019.nt.1	32748.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450	019.nt.1	33066.0	10.7	10.7	10.0	10.0	15.4	15.4	8.0	8.0
DEX0450	019.nt.1	33067.0	14.3	14.3	20.0	20.0	30.8	30.8	8.0	8.0

DEX0450 019.nt.1	35570.0	14.3	14.8	20.0	20.0	30.8	30.8	8.0	8.3
DEX0450 019.nt.1	35571.0	14.3	14.3	30.0	30.0	30.8	30.8	12.0	12.0
DEX0450 019.nt.2	32748.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 019.nt.2	33066.0	10.7	10.7	10.0	10.0	15.4	15.4	8.0	8.0
DEX0450 019.nt.2	33067.0	14.3	14.3	20.0	20.0	30.8	30.8	8.0	8.0
DEX0450 019.nt.2	35570.0	14.3	14.8	20.0	20.0	30.8	30.8	8.0	8.3
DEX0450 019.nt.2	35571.0	14.3	14.3	30.0	30.0	30.8	30.8	12.0	12.0
DEX0450 019.nt.3	32748.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 019.nt.3	33066.0	10.7	10.7	10.0	10.0	15.4	15.4	8.0	8.0
DEX0450 019.nt.3	33067.0	14.3	14.3	20.0	20.0	30.8	30.8	8.0	8.0
DEX0450 019.nt.3	35570.0	14.3	14.8	20.0	20.0	30.8	30.8	8.0	8.3
DEX0450 019.nt.3	35571.0	14.3	14.3	30.0	30.0	30.8	30.8	12.0	12.0
DEX0450 020.nt.1	32972.0	0.0	0.0	30.0	30.0	15.4	15.4	4.0	4.0
DEX0450 020.nt.1	32990.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.1	32991.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.1	32992.0	3.6	3.6	20.0	20.0	7.7	7.7	8.0	8.0
DEX0450 020.nt.1	32994.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.1	32995.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.1	35546.0	3.6	3.6	20.0	20.0	7.7	7.7	8.0	8.0
DEX0450 020.nt.2	32972.0	0.0	0.0	30.0	30.0	15.4	15.4	4.0	4.0
DEX0450 020.nt.2	32990.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.2	32991.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.2	32992.0	3.6	3.6	20.0	20.0	7.7	7.7	8.0	8.0
DEX0450 020.nt.2	32995.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.2	35546.0	3.6	3.6	20.0	20.0	7.7	7.7	8.0	8.0
DEX0450 020.nt.3	32972.0	0.0	0.0	30.0	30.0	15.4	15.4	4.0	4.0
DEX0450 020.nt.3	32990.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.3	32991.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.3	32992.0	3.6	3.6	20.0	20.0	7.7	7.7	8.0	8.0
DEX0450 020.nt.3	32995.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0450 020.nt.3	35546.0	3.6	3.6	20.0	20.0	7.7	7.7	8.0	8.0
DEX0450 021.nt.1	10700.0	3.6	5.9	0.0	0.0	7.7	10.0	0.0	0.0
DEX0450 021.nt.1	10701.0	0.0	0.0	10.0	12.5	7.7	9.1	0.0	0.0
DEX0450 021.nt.1	10744.0	10.7	11.5	30.0	33.3	30.8	30.8	8.0	9.1
DEX0450 021.nt.1	10745.0	3.6	4.3	10.0	12.5	15.4	16.7	0.0	0.0
DEX0450 022.nt.1	12057.0	3.6	3.8	30.0	30.0	30.8	30.8	0.0	0.0
DEX0450 022.nt.1	12058.0	0.0	0.0	10.0	10.0	7.7	7.7	0.0	0.0
DEX0450 023.nt.1	8910.0	25.0	25.0	30.0	30.0	53.8	53.8	12.0	12.0
DEX0450 024.nt.1	36564.0	28.6	28.6	50.0	50.0	61.5	61.5	20.0	20.0
DEX0450 025.nt.1	37705.0	28.6	28.6	20.0	20.0	15.4	15.4	32.0	32.0
DEX0450 025.nt.1	37706.0	25.0	25.0	10.0	10.0	7.7	7.7	28.0	28.0
DEX0450 027.nt.1	35470.0	32.1	32.1	40.0	40.0	30.8	30.8	36.0	36.0
DEX0450 027.nt.1	35471.0	42.9	42.9	40.0	40.0	38.5	38.5	44.0	44.0
DEX0450 027.nt.2	35470.0	32.1	32.1	40.0	40.0	30.8	30.8	36.0	36.0
DEX0450 027.nt.2	35471.0	42.9	42.9	40.0	40.0	38.5	38.5	44.0	44.0
DEX0450 028.nt.1	31539.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 028.nt.1	31545.0	7.1	7.1	30.0	30.0	30.8	30.8	4.0	4.0
DEX0450 030.nt.1	8410.0	14.3	14.3	10.0	10.0	30.8	30.8	4.0	4.0
DEX0450 030.nt.1	8411.0	14.3	14.3	10.0	10.0	30.8	30.8	4.0	4.0
DEX0450 031.nt.1	21356.0	17.9	17.9	20.0	22.2	15.4	16.7	20.0	20.0
DEX0450 031.nt.1	28423.0	10.7	11.1	40.0	40.0	23.1	23.1	16.0	16.7
DEX0450 031.nt.2	21356.0	17.9	17.9	20.0	22.2	15.4	16.7	20.0	20.0
DEX0450 032.nt.1	34888.0	14.3	14.3	30.0	30.0	38.5	38.5	8.0	8.0
DEX0450 033.nt.1	30532.0	35.7	35.7	70.0	70.0	61.5	61.5	36.0	36.0
DEX0450 033.nt.2	34642.0	21.4	25.0	30.0	50.0	23.1	33.3	24.0	28.6
DEX0450 033.nt.2	34643.0	10.7	12.0	50.0	62.5	7.7	10.0	28.0	30.4
DEX0450 034.nt.1	37498.0	0.0	0.0	30.0	30.0	23.1	23.1	0.0	0.0

DEX0450 035.nt.1	20153.0	14.3	14.8	40.0	40.0	38.5	38.5	12.0	12.5
DEX0450 035.nt.1	20154.0	10.7	10.7	0.0	0.0	7.7	7.7	8.0	8.0
DEX0450 036.nt.1	37615.0	46.4	46.4	50.0	50.0	30.8	30.8	56.0	56.0
DEX0450 036.nt.1	37616.0	42.9	42.9	50.0	50.0	30.8	30.8	52.0	52.0
DEX0450 036.nt.1	37635.0	39.3	39.3	50.0	50.0	23.1	23.1	52.0	52.0
DEX0450 037.nt.1	33741.0	46.4	48.1	40.0	44.4	23.1	27.3	56.0	56.0
DEX0450 038.nt.1	38975.0	14.3	14.3	20.0	20.0	15.4	15.4	16.0	16.0
DEX0450 038.nt.1	38976.0	14.3	14.3	30.0	30.0	15.4	15.4	20.0	20.0
DEX0450 039.nt.1	38501.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.1	38502.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.2	36599.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0450 039.nt.2	38428.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0450 039.nt.2	38499.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0450 039.nt.2	38501.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.2	38502.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.2	38509.0	7.1	7.1	0.0	0.0	7.7	7.7	4.0	4.0
DEX0450 039.nt.2	38510.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0450 039.nt.3	36599.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0450 039.nt.3	38428.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0450 039.nt.3	38499.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0450 039.nt.3	38501.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.3	38509.0	7.1	7.1	0.0	0.0	7.7	7.7	4.0	4.0
DEX0450 039.nt.3	38510.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0450 039.nt.4	36599.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0450 039.nt.4	38428.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0450 039.nt.4	38499.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0450 039.nt.4	38501.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.4	38502.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.4	38509.0	7.1	7.1	0.0	0.0	7.7	7.7	4.0	4.0
DEX0450 039.nt.4	38510.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0450 039.nt.5	38501.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.5	38502.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.6	38501.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 039.nt.6	38502.0	7.1	7.1	0.0	0.0	15.4	15.4	0.0	0.0
DEX0450 040.nt.1	35520.0	46.4	46.4	20.0	20.0	46.2	46.2	36.0	36.0
DEX0450 040.nt.1	35521.0	46.4	46.4	30.0	30.0	53.8	53.8	36.0	36.0
DEX0450 040.nt.1	39581.0	35.7	38.5	30.0	30.0	46.2	50.0	28.0	29.2
DEX0450 040.nt.1	39582.0	46.4	46.4	30.0	30.0	53.8	53.8	36.0	36.0
DEX0450 041.nt.1	33072.0	0.0	0.0	10.0	10.0	0.0	0.0	4.0	4.0
DEX0450 041.nt.1	33074.0	7.1	7.4	50.0	50.0	38.5	38.5	8.0	8.3
DEX0450 041.nt.1	33075.0	3.6	3.6	40.0	40.0	30.8	30.8	4.0	4.0
DEX0450 041.nt.1	36755.0	0.0	0.0	20.0	20.0	15.4	15.4	0.0	0.0
DEX0450 041.nt.1	36756.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 041.nt.1	37290.0	3.6	3.6	10.0	10.0	7.7	7.7	4.0	4.0
DEX0450 042.nt.1	33118.0	3.6	3.6	20.0	20.0	23.1	23.1	0.0	0.0
DEX0450 042.nt.1	33119.0	3.6	3.6	10.0	10.0	15.4	15.4	0.0	0.0
DEX0450 042.nt.1	34009.0	21.4	21.4	40.0	44.4	53.8	53.8	12.0	12.5
DEX0450 042.nt.1	40737.0	10.7	10.7	20.0	20.0	30.8	30.8	4.0	4.0
DEX0450 042.nt.2	33118.0	3.6	3.6	20.0	20.0	23.1	23.1	0.0	0.0
DEX0450 042.nt.2	33119.0	3.6	3.6	10.0	10.0	15.4	15.4	0.0	0.0
DEX0450 042.nt.2	34009.0	21.4	21.4	40.0	44.4	53.8	53.8	12.0	12.5
DEX0450 042.nt.2	40737.0	10.7	10.7	20.0	20.0	30.8	30.8	4.0	4.0
DEX0450 043.nt.1	35881.0	0.0	0.0	10.0	12.5	7.7	9.1	0.0	0.0
DEX0450 043.nt.1	35882.0	3.6	25.0	0.0	0.0	0.0	0.0	4.0	25.0
DEX0450 043.nt.1	36669.0	25.0	25.0	40.0	40.0	38.5	38.5	24.0	24.0
DEX0450 043.nt.1	36670.0	25.0	25.0	40.0	40.0	38.5	38.5	24.0	24.0
DEX0450 044.nt.1	9110.0	28.6	28.6	30.0	30.0	23.1	23.1	32.0	32.0

DEX0450 045.nt.1	13783.0	14.3	14.3	20.0	20.0	30.8	30.8	8.0	8.0
DEX0450 045.nt.1	13784.0	14.3	14.3	10.0	10.0	30.8	30.8	4.0	4.0
DEX0450 046.nt.1	10297.0	53.6	53.6	90.0	90.0	84.6	84.6	52.0	52.0
DEX0450 047.nt.1	30511.0	14.3	14.8	50.0	50.0	53.8	53.8	8.0	8.3
DEX0450 047.nt.1	38789.0	7.1	7.1	10.0	10.0	15.4	15.4	4.0	4.0
DEX0450 047.nt.1	39412.0	7.1	7.1	10.0	10.0	15.4	15.4	4.0	4.0
DEX0450 048.nt.1	41177.0	3.6	3.6	20.0	20.0	15.4	15.4	4.0	4.0
DEX0450 048.nt.1	41178.0	3.6	3.7	30.0	30.0	23.1	23.1	4.0	4.2
DEX0450 049.nt.1	31424.0	7.1	8.0	20.0	22.2	23.1	23.1	4.0	4.8
DEX0450 049.nt.1	31425.0	3.6	4.0	30.0	37.5	30.8	30.8	0.0	0.0
DEX0450 050.nt.1	9398.0	28.6	28.6	20.0	20.0	30.8	30.8	24.0	24.0
DEX0450 050.nt.1	9399.0	28.6	28.6	20.0	20.0	30.8	30.8	24.0	24.0
DEX0450 052.nt.1	37943.0	46.4	46.4	70.0	70.0	76.9	76.9	40.0	40.0
DEX0450 052.nt.1	37944.0	42.9	44.4	70.0	70.0	76.9	76.9	36.0	37.5
DEX0450 053.nt.1	9398.0	28.6	28.6	20.0	20.0	30.8	30.8	24.0	24.0
DEX0450 053.nt.1	9399.0	28.6	28.6	20.0	20.0	30.8	30.8	24.0	24.0

Table 3.

DEX ID	Oligo Name	Cln Multi-Cancer ALL %up n=27	Cln Multi-Cancer ALL %valid up n=27	Cln Multi-Cancer ASC %up n=14	Cln Multi-Cancer ASC %valid up n=14	Cln Multi-Cancer RS %up n=13	Cln Multi-Cancer RS %valid up n=13
DEX0450 025.nt.1	77759.0	37.0	37.0	21.4	21.4	53.8	53.8
DEX0450 025.nt.1	77759.1	33.3	33.3	21.4	21.4	46.2	46.2
DEX0450 031.nt.1	956.0	7.4	8.3	14.3	15.4	0.0	0.0

BREAST CANCER CHIPS

- 5 For breast cancer two different chip designs were evaluated with overlapping sets of a total of 36 samples, comparing the expression patterns of breast cancer derived polyA+ RNA to polyA+ RNA isolated from a pool of 10 normal breast tissues. For the Breast Array Chip, all 36 samples (9 stage I cancers, 23 stage II cancers, 4 stage III cancers) were analyzed. These samples also represented 10 Grade1/2 and 26 Grade 3
- 10 cancers. The histopathologic grades for cancer are classified as follows: GX, cannot be assessed; G1, well differentiated; G2, moderately differentiated; G3, poorly differentiated; and G4, undifferentiated. AJCC Cancer Staging Handbook, pp. 9, (5th Ed, 1998). Samples were further grouped based on the expression patterns of the known breast cancer associated genes Her2 and ER α (10 HER2 up, 26 HER2 not up, 20 ER up and 16 ER not
- 15 up) and for the Multi-Cancer Array Chip, a subset of 20 of these samples (9 stage I cancers, 8 stage II cancers, 3 stage III cancers) were assessed.

The results for the statistically significant up-regulated genes on the Breast Array Chip are shown in Tables 4 and 5. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 6. The first two

columns of each table contain information about the sequence itself (Seq ID, Oligo Name), the next columns show the results obtained for all ("ALL") breast cancer samples, cancers corresponding to stage I ("ST1"), stages II and III ("ST2,3"), grades 1 and 2 ("GR1,2"), grade 3 ("GR3"), cancers exhibiting up-regulation of Her2 ("HER2up") or ER α ("ERup") or those not exhibiting up-regulation of Her2 ("NOT HER2up") or ER α ("NOT ERup"). '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed (n=36 for Colon Array Chip, n=20 for the Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

10 Table 4.

[illegible]

[illegible]

[illegible]

[illegible]

DEX0450_03 2.nt.7	19576.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_03 2.nt.7	20237.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_03 2.nt.7	31590.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_03 2.nt.7	31591.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_04 4.nt.1	24210.0	2.8	2.8	11.1	11.1	0.0	0.0	0.0	0.0	3.8	3.8
DEX0450_04 4.nt.1	24211.0	5.6	5.6	11.1	11.1	3.7	3.7	0.0	0.0	7.7	7.7
DEX0450_04 4.nt.2	24210.0	2.8	2.8	11.1	11.1	0.0	0.0	0.0	0.0	3.8	3.8
DEX0450_04 4.nt.2	24211.0	5.6	5.6	11.1	11.1	3.7	3.7	0.0	0.0	7.7	7.7
DEX0450_04 4.nt.3	24210.0	2.8	2.8	11.1	11.1	0.0	0.0	0.0	0.0	3.8	3.8
DEX0450_04 4.nt.3	24211.0	5.6	5.6	11.1	11.1	3.7	3.7	0.0	0.0	7.7	7.7
DEX0450_04 5.nt.1	19853.0	5.6	5.6	0.0	0.0	7.4	7.4	0.0	0.0	7.7	7.7
DEX0450_04 5.nt.1	19854.0	2.8	2.8	0.0	0.0	3.7	3.7	0.0	0.0	3.8	3.8
DEX0450_05 3.nt.1	31644.0	19.4	19.4	22.2	22.2	18.5	18.5	20.0	20.0	19.2	19.2
DEX0450_05 3.nt.1	31645.0	19.4	19.4	22.2	22.2	18.5	18.5	20.0	20.0	19.2	19.2

Table 5.

[illegible]

[illegible]

DEX0450 032.nt.6	15315.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	15320.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	15324.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	15829.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	15830.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	15848.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	15865.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	16111.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	16906.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	16908.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	16910.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	16912.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	19576.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	20237.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	31590.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	31591.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	15315.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	15317.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	15320.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	15324.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	15848.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	15865.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	16906.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	16908.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	16912.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	19576.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	20237.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	31590.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	31591.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 044.nt.1	24210.0	0.0	0.0	3.8	3.8	0.0	0.0	6.2	6.2
DEX0450 044.nt.1	24211.0	10.0	10.0	3.8	3.8	5.0	5.0	6.2	6.2
DEX0450 044.nt.2	24210.0	0.0	0.0	3.8	3.8	0.0	0.0	6.2	6.2
DEX0450 044.nt.2	24211.0	10.0	10.0	3.8	3.8	5.0	5.0	6.2	6.2
DEX0450 044.nt.3	24210.0	0.0	0.0	3.8	3.8	0.0	0.0	6.2	6.2
DEX0450 044.nt.3	24211.0	10.0	10.0	3.8	3.8	5.0	5.0	6.2	6.2
DEX0450 045.nt.1	19853.0	0.0	0.0	7.7	7.7	0.0	0.0	12.5	12.5
DEX0450 045.nt.1	19854.0	0.0	0.0	3.8	3.8	0.0	0.0	6.2	6.2
DEX0450 053.nt.1	31644.0	0.0	0.0	26.9	26.9	15.0	15.0	25.0	25.0
DEX0450 053.nt.1	31645.0	0.0	0.0	26.9	26.9	15.0	15.0	25.0	25.0

Table 6.

DEX ID	Oligo Name	Mam Multi-Cancer ALL %up n=20	Mam Multi-Cancer ALL %valid up n=20	Mam Multi-Cancer ST1 %up n=9	Mam Multi-Cancer ST1 %valid up n=9	Mam Multi-Cancer ST2,3 %up n=11	Mam Multi-Cancer ST2,3 %valid up n=11
DEX0450 025.nt.1	77759.0	15.0	15.0	11.1	11.1	18.2	18.2
DEX0450 025.nt.1	77759.1	15.0	15.0	11.1	11.1	18.2	18.2
DEX0450 031.nt.1	956.0	5.0	5.0	11.1	11.1	0.0	0.0

LUNG CANCER CHIPS

- 5 For lung cancer two different chip designs were evaluated with overlapping sets of a total of 29 samples, comparing the expression patterns of lung cancer derived polyA+

RNA to polyA+ RNA isolated from a pool of 12 normal lung tissues. For the Lung Array Chip all 29 samples (15 squamous cell carcinomas and 14 adenocarcinomas including 14 stage I and 15 stage II/III cancers) were analyzed and for the Multi-Cancer Array Chip a subset of 22 of these samples (10 squamous cell carcinomas, 12 adenocarcinomas) were assessed.

The results for the statistically significant up-regulated genes on the Lung Array Chip are shown in Table 7. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 8. The first two columns of each table contain information about the sequence itself (DEX ID, Oligo Name), the next 10 columns show the results obtained for all ("ALL") lung cancer samples, squamous cell carcinomas ("SQ"), adenocarcinomas ("AD"), or cancers corresponding to stage I ("ST1"), or stages II and III ("ST2,3"). '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed (n=29 for Lung Array Chip, n=22 for Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with 15 valid expression values in which up-regulation of at least 2-fold was observed.

Table 7.

[illegible]

DEX0450_031.nt.1	5750.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_031.nt.2	957.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_031.nt.2	5254.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_031.nt.2	5749.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_031.nt.2	5750.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_033.nt.1	1234.0	51.7	51.7	80.0	80.0	21.4	21.4	57.1	57.1	46.7	46.7
DEX0450_033.nt.2	5421.0	44.8	44.8	33.3	33.3	57.1	57.1	35.7	35.7	53.3	53.3
DEX0450_036.nt.1	5961.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_037.nt.1	1022.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_037.nt.1	1023.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450_045.nt.1	5599.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 8.

DEX ID	Oligo Name	Lng Multi-Cancer ALL %up n=22	Lng Multi-Cancer ALL %valid up n=22	Lng Multi-Cancer SQ %up n=10	Lng Multi-Cancer SQ %valid up n=10	Lng Multi-Cancer AD %up n=12	Lng Multi-Cancer AD %valid up n=12
DEX0450_025.nt.1	77759.0	31.8	33.3	30.0	30.0	33.3	36.4
DEX0450_025.nt.1	77759.1	50.0	50.0	50.0	50.0	50.0	50.0
DEX0450_031.nt.1	956.0	0.0	0.0	0.0	0.0	0.0	0.0

OVARIAN CANCER CHIPS

- 5 For ovarian cancer two different chip designs were evaluated with overlapping sets of a total of 19 samples, comparing the expression patterns of ovarian cancer derived total RNA to total RNA isolated from a pool of 9 normal ovarian tissues. For the Multi-Cancer Array Chip, all 19 samples (14 invasive carcinomas, 5 low malignant potential samples were analyzed and for the Ovarian Array Chip, a subset of 17 of these samples (13
- 10 invasive carcinomas, 4 low malignant potential samples) were assessed.

- The results for the statistically significant up-regulated genes on the Ovarian Array Chip are shown in Table 9. The results for the Multi-Cancer Array Chip are shown in Table 10. The first two columns of each table contain information about the sequence itself (DEX ID, Oligo Name), the next columns show the results obtained for all ("ALL")
- 15 ovarian cancer samples, invasive carcinomas ("INV") and low malignant potential ("LMP") samples. '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed (n=19 for the Multi-Cancer Array Chip, n=17

for the Ovarian Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

Table 9.

DEX ID	Oligo Name	Ovr ALL %up n=17	Ovr ALL %valid up n=17	Ovr INV %up n=13	Ovr INV %valid up n=13	Ovr LMP %up n=4	Ovr LMP %valid up n=4
DEX0450 029.nt.1	37947.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 029.nt.1	37947.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0450 031.nt.1	9880.01	17.6	21.4	15.4	18.2	25.0	33.3
DEX0450 031.nt.1	9880.02	17.6	18.8	15.4	16.7	25.0	25.0
DEX0450 033.nt.1	18480.01	88.2	88.2	92.3	92.3	75.0	75.0
DEX0450 033.nt.1	18480.02	88.2	88.2	92.3	92.3	75.0	75.0
DEX0450 033.nt.2	18480.01	88.2	88.2	92.3	92.3	75.0	75.0
DEX0450 033.nt.2	18480.02	88.2	88.2	92.3	92.3	75.0	75.0
DEX0450 037.nt.1	12335.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0450 037.nt.1	12335.02	5.9	5.9	7.7	7.7	0.0	0.0

5 Table 10.

DEX ID	Oligo Name	Ovr Multi-Cancer ALL %up n=19	Ovr Multi-Cancer ALL %valid up n=19	Ovr Multi-Cancer INV %up n=14	Ovr Multi-Cancer INV %valid up n=14	Ovr Multi-Cancer LMP %up n=5	Ovr Multi-Cancer LMP %valid up n=5
DEX0450 025.nt.1	77759.0	5.3	5.9	7.1	7.7	0.0	0.0
DEX0450 025.nt.1	77759.1	5.3	6.2	7.1	8.3	0.0	0.0
DEX0450 031.nt.1	956.0	10.5	15.4	7.1	11.1	20.0	25.0

PROSTATE CANCER

For prostate cancer three different chip designs were evaluated with overlapping sets of a total of 29 samples, comparing the expression patterns of prostate cancer or benign disease derived total RNA to total RNA isolated from a pool of 35 normal prostate tissues. For the Prostate1 Array and Prostate2 Array Chips all 29 samples (17 prostate cancer samples, 12 non-malignant disease samples) were analyzed. For the Multi-Cancer Array Chip a subset of 28 of these samples (16 prostate cancer samples, 12 non-malignant disease samples) were analyzed.

The results for the statistically significant up-regulated genes on the Prostate1 Array Chip and the Prostate2 Array Chip are shown in Table 11. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 12. The first two columns of each table contain information about the sequence itself (DEX ID, Oligo Name), the next columns show the results obtained for prostate cancer samples ("CAN") or non-malignant disease samples ("DIS"). '%up' indicates the

percentage of all experiments in which up-regulation of at least 2-fold was observed (n=29 for the Prostate2 Array Chip and the Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

5 Table 11.

DEX ID	Oligo Name	Pro CAN %up n=17	Pro CAN %valid up n=17	Pro DIS %up n=12	Pro DIS %valid up n=12
DEX0450 031.nt.1	38723.02	0.0	0.0	0.0	0.0
DEX0450 031.nt.1	38723.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	32036.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	32036.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35907.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35907.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35907.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35945.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35945.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35945.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35955.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35955.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.1	35955.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	26953.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	26953.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	31256.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	31256.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	31256.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	32020.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	32020.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	32036.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	32036.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35897.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35897.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35897.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35901.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35901.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35901.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35905.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35905.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35905.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35907.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35907.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35907.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35919.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35919.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35919.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35945.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35945.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35945.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35951.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35951.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35951.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35955.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35955.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35955.03	0.0	0.0	0.0	0.0

DEX0450 032.nt.2	35957.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35957.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35957.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35959.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35959.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.2	35959.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	26953.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	26953.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	31256.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	31256.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	31256.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	32020.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	32020.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	32036.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	32036.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35897.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35897.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35897.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35901.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35901.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35901.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35905.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35905.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35905.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35907.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35907.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35907.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35919.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35919.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35919.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35945.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35945.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35945.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35951.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35951.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35951.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35955.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35955.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35955.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35957.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35957.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35957.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35959.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35959.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.3	35959.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	26953.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	26953.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	31256.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	31256.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	31256.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	32020.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	32020.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	32036.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	32036.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	35897.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	35897.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.4	35897.03	0.0	0.0	0.0	0.0

DEX0450	032.nt.4	35901.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35901.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35901.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35905.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35905.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35905.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35907.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35907.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35907.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35919.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35919.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35919.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35945.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35945.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35945.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35951.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35951.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35951.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35955.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35955.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35955.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35957.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35957.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35957.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35959.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35959.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.4	35959.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	26953.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	26953.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	31256.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	31256.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	31256.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	32020.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	32020.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	32036.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	32036.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35897.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35897.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35897.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35901.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35901.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35901.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35905.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35905.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35905.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35907.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35907.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35907.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35919.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35919.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35919.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35945.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35945.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35945.03	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35951.01	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35951.02	0.0	0.0	0.0	0.0
DEX0450	032.nt.5	35951.03	0.0	0.0	0.0	0.0

DEX0450 032.nt.5	35955.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35955.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35955.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35957.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35957.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35957.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35959.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35959.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.5	35959.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	26953.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	26953.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	31256.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	31256.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	31256.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	32020.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	32020.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	32036.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	32036.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35897.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35897.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35897.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35901.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35901.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35901.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35905.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35905.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35905.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35907.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35907.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35907.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35919.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35919.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35919.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35945.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35945.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35945.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35951.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35951.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35951.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35955.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35955.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35955.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35957.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35957.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35957.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35959.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35959.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.6	35959.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	26953.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	26953.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	31256.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	31256.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	31256.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	32020.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	32020.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	32036.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	32036.02	0.0	0.0	0.0	0.0

DEX0450 032.nt.7	35901.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35901.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35901.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35905.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35905.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35905.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35907.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35907.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35907.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35919.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35919.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35919.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35945.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35945.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35945.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35951.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35951.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35951.03	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35955.01	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35955.02	0.0	0.0	0.0	0.0
DEX0450 032.nt.7	35955.03	0.0	0.0	0.0	0.0
DEX0450 033.nt.2	24954.01	0.0	0.0	0.0	0.0
DEX0450 033.nt.2	24954.02	0.0	0.0	0.0	0.0
DEX0450 033.nt.2	28019.01	5.9	5.9	0.0	0.0
DEX0450 033.nt.2	28019.02	0.0	0.0	0.0	0.0
DEX0450 037.nt.1	29065.01	0.0	0.0	8.3	8.3
DEX0450 037.nt.1	29065.02	0.0	0.0	8.3	8.3
DEX0450 037.nt.1	29065.03	0.0	0.0	8.3	8.3
DEX0450 037.nt.1	29069.01	0.0	0.0	0.0	0.0
DEX0450 037.nt.1	29069.02	0.0	0.0	0.0	0.0
DEX0450 037.nt.1	29069.03	0.0	0.0	0.0	0.0
DEX0450 037.nt.1	36689.01	0.0	0.0	0.0	0.0
DEX0450 037.nt.1	36689.02	0.0	0.0	0.0	0.0
DEX0450 041.nt.1	29311.01	0.0	0.0	0.0	0.0
DEX0450 041.nt.1	29311.02	0.0	0.0	0.0	0.0
DEX0450 041.nt.1	29311.03	0.0	0.0	0.0	0.0
DEX0450 041.nt.1	29313.01	0.0	0.0	0.0	0.0
DEX0450 041.nt.1	29313.02	0.0	0.0	0.0	0.0
DEX0450 041.nt.1	29313.03	0.0	0.0	0.0	0.0

Table 12.

DEX ID	Oligo Name	Pro Multi-Cancer CAN %up n=16	Pro Multi-Cancer CAN %valid up n=16	Pro Multi-Cancer DIS %up n=12	Pro Multi-Cancer DIS %valid up n=12
DEX0450 025.nt.1	77759.0	0.0	0.0	0.0	0.0
DEX0450 025.nt.1	77759.1	0.0	0.0	0.0	0.0
DEX0450 031.nt.1	956.0	0.0	0.0	0.0	0.0

- SEQ ID NO: 1-94 was up-regulated on various tissue microarrays. Accordingly,
- 5 nucleotide SEQ ID NO: 1-94 or the encoded protein SEQ ID NO: 95-248 may be used as a cancer therapeutic and/or diagnostic target for the tissues in which expression is shown.

The following table lists the location (Oligo Location) where the microarray oligos (Oligo ID) map on the transcripts (DEX ID) of the present invention. Each Oligo ID may have been printed multiple times on a single chip as replicates. The Oligo Name is an exemplary replicate (e.g. 1000.01) for the Oligo ID (e.g. 1000), and data from other replicates (e.g. 1000.02, 1000.03) may be reported. Additionally, the Array (Chip Name) that each oligo and oligo replicates were printed on is included.

DEX ID	Oligo ID	Oligo Name	Chip Name	Oligo Location
DEX0450 001.nt.1	2383	2383.0	Lung array	1925-1984
DEX0450 001.nt.1	4832	4832.0	Lung array	1101-1160
DEX0450 001.nt.1	4831	4831.0	Lung array	376-435
DEX0450 001.nt.1	2404	2404.0	Lung array	1925-1984
DEX0450 001.nt.1	2405	2405.0	Multi-Cancer array	1918-1977
DEX0450 001.nt.1	2400	2400.0	Lung array	611-670
DEX0450 002.nt.1	31163	31163.0	Colon array	1644-1703
DEX0450 002.nt.1	34075	34075.0	Colon array	2521-2580
DEX0450 002.nt.1	31158	31158.0	Colon array	2221-2280
DEX0450 002.nt.1	31162	31162.0	Colon array	1666-1725
DEX0450 002.nt.1	31003	31003.0	Colon array	1156-1215
DEX0450 002.nt.1	34074	34074.0	Colon array	2597-2656
DEX0450 002.nt.1	31159	31159.0	Colon array	2168-2227
DEX0450 003.nt.1	31446	31446.0	Colon array	37-96
DEX0450 003.nt.2	31447	31447.0	Colon array	3391-3450
DEX0450 003.nt.2	31446	31446.0	Colon array	3635-3694
DEX0450 003.nt.3	31447	31447.0	Colon array	2288-2347
DEX0450 003.nt.3	31443	31443.0	Colon array	1628-1687
DEX0450 004.nt.1	10720	10720.0	Colon array	260-319
DEX0450 004.nt.1	10721	10721.0	Colon array	220-279
DEX0450 005.nt.1	38049	38049.0	Colon array	2673-2732
DEX0450 005.nt.1	16776	16776.0	Colon array	422-481
DEX0450 005.nt.1	16777	16777.0	Colon array	336-395
DEX0450 005.nt.1	38050	38050.0	Colon array	2564-2623
DEX0450 006.nt.1	35170	35170.0	Colon array	511-570
DEX0450 006.nt.1	35171	35171.0	Colon array	461-520
DEX0450 007.nt.1	35170	35170.0	Colon array	3353-3412
DEX0450 008.nt.1	30228	30228.0	Colon array	2517-2576
DEX0450 008.nt.1	30227	30227.0	Colon array	2563-2622
DEX0450 009.nt.1	39839	39839.0	Colon array	975-1034
DEX0450 009.nt.1	39840	39840.0	Colon array	822-881
DEX0450 009.nt.2	39839	39839.0	Colon array	1702-1761
DEX0450 009.nt.2	39840	39840.0	Colon array	1549-1608
DEX0450 010.nt.1	29571	29571.0	Colon array	79-138
DEX0450 010.nt.1	29612	29612.0	Colon array	456-515
DEX0450 010.nt.1	29595	29595.0	Colon array	493-552
DEX0450 010.nt.1	29609	29609.0	Colon array	486-545
DEX0450 010.nt.1	22376	22376.0	Breast array	482-541
DEX0450 010.nt.1	29582	29582.0	Colon array	482-541
DEX0450 010.nt.1	29611	29611.0	Colon array	493-552
DEX0450 010.nt.1	17829	17829.0	Breast array	87-146
DEX0450 010.nt.2	29611	29611.0	Colon array	299-358
DEX0450 010.nt.2	29595	29595.0	Colon array	299-358
DEX0450 010.nt.2	22376	22376.0	Breast array	288-347
DEX0450 010.nt.2	29582	29582.0	Colon array	288-347

DEX0450 010.nt.2	29609	29609.0	Colon array	292-351
DEX0450 010.nt.2	29612	29612.0	Colon array	262-321
DEX0450 010.nt.3	36747	36747.0	Colon array	2355-2414
DEX0450 010.nt.3	29595	29595.0	Colon array	4246-4305
DEX0450 010.nt.3	29612	29612.0	Colon array	4209-4268
DEX0450 010.nt.3	29582	29582.0	Colon array	4235-4294
DEX0450 010.nt.3	29572	29572.0	Colon array	3762-3821
DEX0450 010.nt.3	29611	29611.0	Colon array	4246-4305
DEX0450 010.nt.3	17829	17829.0	Breast array	3840-3899
DEX0450 010.nt.3	29571	29571.0	Colon array	3832-3891
DEX0450 010.nt.3	29609	29609.0	Colon array	4239-4298
DEX0450 010.nt.3	22376	22376.0	Breast array	4235-4294
DEX0450 011.nt.1	22654	22654.0	Colon array	1967-2026
DEX0450 012.nt.1	8377	8377.0	Colon array	406-465
DEX0450 013.nt.1	32221	32221.0	Colon array	1359-1418
DEX0450 013.nt.1	32254	32254.0	Colon array	390-449
DEX0450 013.nt.1	33033	33033.0	Colon array	635-694
DEX0450 013.nt.1	32255	32255.0	Colon array	266-325
DEX0450 013.nt.1	32220	32220.0	Colon array	1399-1458
DEX0450 014.nt.1	32458	32458.0	Colon array	1846-1905
DEX0450 014.nt.1	32459	32459.0	Colon array	1806-1865
DEX0450 015.nt.1	33503	33503.0	Colon array	7026-7085
DEX0450 016.nt.1	35091	35091.0	Colon array	3392-3451
DEX0450 016.nt.1	33083	33083.0	Colon array	2718-2777
DEX0450 016.nt.2	35091	35091.0	Colon array	2518-2577
DEX0450 016.nt.3	33083	33083.0	Colon array	2835-2894
DEX0450 016.nt.3	35091	35091.0	Colon array	3509-3568
DEX0450 017.nt.1	36711	36711.0	Colon array	484-543
DEX0450 017.nt.1	39770	39770.0	Colon array	486-545
DEX0450 017.nt.1	39635	39635.0	Colon array	652-711
DEX0450 017.nt.1	36712	36712.0	Colon array	342-401
DEX0450 017.nt.1	39769	39769.0	Colon array	526-585
DEX0450 017.nt.1	39631	39631.0	Colon array	651-710
DEX0450 017.nt.1	39636	39636.0	Colon array	612-671
DEX0450 017.nt.2	39770	39770.0	Colon array	266-325
DEX0450 017.nt.2	39769	39769.0	Colon array	306-365
DEX0450 017.nt.2	36711	36711.0	Colon array	264-323
DEX0450 017.nt.2	39631	39631.0	Colon array	431-490
DEX0450 017.nt.2	39635	39635.0	Colon array	432-491
DEX0450 017.nt.3	39636	39636.0	Colon array	479-538
DEX0450 017.nt.3	39631	39631.0	Colon array	518-577
DEX0450 017.nt.3	39769	39769.0	Colon array	393-452
DEX0450 017.nt.3	39635	39635.0	Colon array	519-578
DEX0450 018.nt.1	31424	31424.0	Colon array	2191-2250
DEX0450 018.nt.1	31425	31425.0	Colon array	2120-2179
DEX0450 018.nt.2	31424	31424.0	Colon array	2191-2250
DEX0450 018.nt.3	31425	31425.0	Colon array	2120-2179
DEX0450 018.nt.3	31424	31424.0	Colon array	2191-2250
DEX0450 018.nt.4	31425	31425.0	Colon array	506-565
DEX0450 019.nt.1	35571	35571.0	Colon array	1385-1444
DEX0450 019.nt.1	32748	32748.0	Colon array	752-811
DEX0450 019.nt.1	33067	33067.0	Colon array	1441-1500
DEX0450 019.nt.1	35570	35570.0	Colon array	1437-1496
DEX0450 019.nt.1	33066	33066.0	Colon array	1531-1590
DEX0450 019.nt.2	35571	35571.0	Colon array	1385-1444
DEX0450 019.nt.2	33067	33067.0	Colon array	1441-1500
DEX0450 019.nt.2	32748	32748.0	Colon array	752-811

DEX0450	019.nt.2	33066	33066.0	Colon array	1531-1590
DEX0450	019.nt.2	35570	35570.0	Colon array	1437-1496
DEX0450	019.nt.3	32748	32748.0	Colon array	752-811
DEX0450	019.nt.3	33067	33067.0	Colon array	1441-1500
DEX0450	019.nt.3	33066	33066.0	Colon array	1531-1590
DEX0450	019.nt.3	35571	35571.0	Colon array	1385-1444
DEX0450	020.nt.1	32972	32972.0	Colon array	1059-1118
DEX0450	020.nt.1	32991	32991.0	Colon array	1226-1285
DEX0450	020.nt.1	32992	32992.0	Colon array	1557-1616
DEX0450	020.nt.1	32990	32990.0	Colon array	1246-1305
DEX0450	020.nt.1	32995	32995.0	Colon array	1100-1159
DEX0450	020.nt.1	32994	32994.0	Colon array	1130-1189
DEX0450	020.nt.1	35546	35546.0	Colon array	1557-1616
DEX0450	020.nt.2	32991	32991.0	Colon array	1885-1944
DEX0450	020.nt.2	32972	32972.0	Colon array	1718-1777
DEX0450	020.nt.2	32992	32992.0	Colon array	2216-2275
DEX0450	020.nt.2	32995	32995.0	Colon array	1759-1818
DEX0450	020.nt.2	32990	32990.0	Colon array	1905-1964
DEX0450	020.nt.3	32995	32995.0	Colon array	4462-4521
DEX0450	020.nt.3	32992	32992.0	Colon array	4919-4978
DEX0450	020.nt.3	32991	32991.0	Colon array	4588-4647
DEX0450	020.nt.3	32990	32990.0	Colon array	4608-4667
DEX0450	020.nt.3	35546	35546.0	Colon array	4919-4978
DEX0450	020.nt.3	32972	32972.0	Colon array	4421-4480
DEX0450	021.nt.1	10701	10701.0	Colon array	3600-3659
DEX0450	021.nt.1	10744	10744.0	Colon array	4464-4523
DEX0450	021.nt.1	10745	10745.0	Colon array	4424-4483
DEX0450	021.nt.1	10700	10700.0	Colon array	3685-3744
DEX0450	022.nt.1	12058	12058.0	Colon array	975-1034
DEX0450	022.nt.1	12057	12057.0	Colon array	1271-1330
DEX0450	023.nt.1	22060	22060.0	Breast array	1652-1711
DEX0450	023.nt.1	8910	8910.0	Colon array	1898-1957
DEX0450	023.nt.2	22060	22060.0	Breast array	776-835
DEX0450	023.nt.3	8910	8910.0	Colon array	381-440
DEX0450	024.nt.1	36564	36564.0	Colon array	315-374
DEX0450	025.nt.1	37705	37705.0	Colon array	273-332
DEX0450	025.nt.1	77759	77759.0	Multi-Cancer array	46-105
DEX0450	025.nt.1	37706	37706.0	Colon array	233-292
DEX0450	027.nt.1	35471	35471.0	Colon array	2662-2721
DEX0450	027.nt.1	35470	35470.0	Colon array	2787-2846
DEX0450	027.nt.2	35471	35471.0	Colon array	2708-2767
DEX0450	028.nt.1	31539	31539.0	Colon array	715-774
DEX0450	028.nt.1	31545	31545.0	Colon array	938-997
DEX0450	029.nt.1	37947	37947.02	Ovarian array	1100-1159
DEX0450	030.nt.1	8410	8410.0	Colon array	174-233
DEX0450	030.nt.1	8411	8411.0	Colon array	144-203
DEX0450	031.nt.1	957	957.0	Lung array	1843-1902
DEX0450	031.nt.1	28423	28423.0	Colon array	284-343
DEX0450	031.nt.1	956	956.0	Multi-Cancer array	280-339
DEX0450	031.nt.1	17869	17869.0	Breast array	279-338
DEX0450	031.nt.1	9880	9880.01	Ovarian array	284-343
DEX0450	031.nt.1	31466	31466.0	Breast array	648-707
DEX0450	031.nt.1	955	955.0	Lung array	285-344
DEX0450	031.nt.1	38723	38723.01	Prostate2 array	285-344
DEX0450	031.nt.1	5750	5750.0	Lung array	1882-1941
DEX0450	031.nt.1	835	835.0	Lung array	638-697
DEX0450	031.nt.1	21356	21356.0	Colon array	2168-2227

DEX0450	031.nt.1	5254	5254.0	Lung array	2168-2227
DEX0450	031.nt.1	836	836.0	Lung array	618-677
DEX0450	031.nt.1	5749	5749.0	Lung array	1767-1826
DEX0450	031.nt.1	953	953.0	Lung array	478-537
DEX0450	031.nt.2	5749	5749.0	Lung array	442-501
DEX0450	031.nt.2	5750	5750.0	Lung array	557-616
DEX0450	031.nt.2	957	957.0	Lung array	518-577
DEX0450	031.nt.2	5254	5254.0	Lung array	843-902
DEX0450	031.nt.2	21356	21356.0	Colon array	843-902
DEX0450	032.nt.1	35945	35945.03	Prostate2 array	851-910
DEX0450	032.nt.1	15848	15848.0	Breast array	942-1001
DEX0450	032.nt.1	35955	35955.02	Prostate2 array	942-1001
DEX0450	032.nt.1	32036	32036.02	Prostate1 array	942-1001
DEX0450	032.nt.1	19576	19576.0	Breast array	942-1001
DEX0450	032.nt.1	16912	16912.0	Breast array	851-910
DEX0450	032.nt.1	35907	35907.03	Prostate2 array	851-910
DEX0450	032.nt.1	34888	34888.0	Colon array	965-1024
DEX0450	032.nt.1	16908	16908.0	Breast array	942-1001
DEX0450	032.nt.2	16912	16912.0	Breast array	5212-5271
DEX0450	032.nt.2	16111	16111.0	Breast array	4379-4438
DEX0450	032.nt.2	35897	35897.03	Prostate2 array	3910-3969
DEX0450	032.nt.2	35959	35959.02	Prostate2 array	4379-4438
DEX0450	032.nt.2	15320	15320.0	Breast array	3570-3629
DEX0450	032.nt.2	31256	31256.03	Prostate2 array	3565-3624
DEX0450	032.nt.2	35907	35907.03	Prostate2 array	5212-5271
DEX0450	032.nt.2	15865	15865.0	Breast array	3565-3624
DEX0450	032.nt.2	16908	16908.0	Breast array	5303-5362
DEX0450	032.nt.2	15848	15848.0	Breast array	5303-5362
DEX0450	032.nt.2	32036	32036.02	Prostate1 array	5303-5362
DEX0450	032.nt.2	15317	15317.0	Breast array	5036-5095
DEX0450	032.nt.2	15315	15315.0	Breast array	4823-4882
DEX0450	032.nt.2	35955	35955.02	Prostate2 array	5303-5362
DEX0450	032.nt.2	16910	16910.0	Breast array	4379-4438
DEX0450	032.nt.2	35945	35945.03	Prostate2 array	5212-5271
DEX0450	032.nt.2	32020	32020.02	Prostate1 array	1062-1121
DEX0450	032.nt.2	35957	35957.03	Prostate2 array	4379-4438
DEX0450	032.nt.2	15324	15324.0	Breast array	4113-4172
DEX0450	032.nt.2	19576	19576.0	Breast array	5303-5362
DEX0450	032.nt.2	35919	35919.02	Prostate2 array	4113-4172
DEX0450	032.nt.2	34888	34888.0	Colon array	5326-5385
DEX0450	032.nt.2	35905	35905.03	Prostate2 array	4833-4892
DEX0450	032.nt.2	26953	26953.02	Prostate1 array	3763-3822
DEX0450	032.nt.2	20237	20237.0	Breast array	1062-1121
DEX0450	032.nt.2	31591	31591.0	Breast array	3572-3631
DEX0450	032.nt.2	35951	35951.01	Prostate2 array	3574-3633
DEX0450	032.nt.2	15830	15830.0	Breast array	3880-3939
DEX0450	032.nt.2	15829	15829.0	Breast array	3910-3969
DEX0450	032.nt.2	16906	16906.0	Breast array	3574-3633
DEX0450	032.nt.2	31590	31590.0	Breast array	3763-3822
DEX0450	032.nt.2	35901	35901.01	Prostate2 array	3570-3629
DEX0450	032.nt.3	35919	35919.02	Prostate2 array	4897-4956
DEX0450	032.nt.3	16111	16111.0	Breast array	5163-5222
DEX0450	032.nt.3	31256	31256.03	Prostate2 array	4349-4408
DEX0450	032.nt.3	15848	15848.0	Breast array	6087-6146
DEX0450	032.nt.3	32036	32036.02	Prostate1 array	6087-6146
DEX0450	032.nt.3	26953	26953.02	Prostate1 array	4547-4606
DEX0450	032.nt.3	35955	35955.02	Prostate2 array	6087-6146

DEX0450 032.nt.3	15315	15315.0	Breast array	5607-5666
DEX0450 032.nt.3	35951	35951.01	Prostate2 array	4358-4417
DEX0450 032.nt.3	15830	15830.0	Breast array	4664-4723
DEX0450 032.nt.3	35901	35901.01	Prostate2 array	4354-4413
DEX0450 032.nt.3	35897	35897.03	Prostate2 array	4694-4753
DEX0450 032.nt.3	35957	35957.03	Prostate2 array	5163-5222
DEX0450 032.nt.3	35945	35945.03	Prostate2 array	5996-6055
DEX0450 032.nt.3	32020	32020.02	Prostate1 array	1062-1121
DEX0450 032.nt.3	35959	35959.02	Prostate2 array	5163-5222
DEX0450 032.nt.3	15324	15324.0	Breast array	4897-4956
DEX0450 032.nt.3	19576	19576.0	Breast array	6087-6146
DEX0450 032.nt.3	15320	15320.0	Breast array	4354-4413
DEX0450 032.nt.3	16908	16908.0	Breast array	6087-6146
DEX0450 032.nt.3	34888	34888.0	Colon array	6110-6169
DEX0450 032.nt.3	15317	15317.0	Breast array	5820-5879
DEX0450 032.nt.3	35905	35905.03	Prostate2 array	5617-5676
DEX0450 032.nt.3	35907	35907.03	Prostate2 array	5996-6055
DEX0450 032.nt.3	15865	15865.0	Breast array	4349-4408
DEX0450 032.nt.3	20237	20237.0	Breast array	1062-1121
DEX0450 032.nt.3	31591	31591.0	Breast array	4356-4415
DEX0450 032.nt.3	15829	15829.0	Breast array	4694-4753
DEX0450 032.nt.3	16910	16910.0	Breast array	5163-5222
DEX0450 032.nt.3	16906	16906.0	Breast array	4358-4417
DEX0450 032.nt.3	31590	31590.0	Breast array	4547-4606
DEX0450 032.nt.3	16912	16912.0	Breast array	5996-6055
DEX0450 032.nt.4	35897	35897.03	Prostate2 array	1668-1727
DEX0450 032.nt.4	15320	15320.0	Breast array	1328-1387
DEX0450 032.nt.4	16111	16111.0	Breast array	2137-2196
DEX0450 032.nt.4	35959	35959.02	Prostate2 array	2137-2196
DEX0450 032.nt.4	16908	16908.0	Breast array	3061-3120
DEX0450 032.nt.4	31256	31256.03	Prostate2 array	1323-1382
DEX0450 032.nt.4	15848	15848.0	Breast array	3061-3120
DEX0450 032.nt.4	32036	32036.02	Prostate1 array	3061-3120
DEX0450 032.nt.4	15865	15865.0	Breast array	1323-1382
DEX0450 032.nt.4	35907	35907.03	Prostate2 array	2970-3029
DEX0450 032.nt.4	15317	15317.0	Breast array	2794-2853
DEX0450 032.nt.4	35955	35955.02	Prostate2 array	3061-3120
DEX0450 032.nt.4	16910	16910.0	Breast array	2137-2196
DEX0450 032.nt.4	15315	15315.0	Breast array	2581-2640
DEX0450 032.nt.4	35945	35945.03	Prostate2 array	2970-3029
DEX0450 032.nt.4	35957	35957.03	Prostate2 array	2137-2196
DEX0450 032.nt.4	32020	32020.02	Prostate1 array	1062-1121
DEX0450 032.nt.4	15324	15324.0	Breast array	1871-1930
DEX0450 032.nt.4	35919	35919.02	Prostate2 array	1871-1930
DEX0450 032.nt.4	19576	19576.0	Breast array	3061-3120
DEX0450 032.nt.4	34888	34888.0	Colon array	3084-3143
DEX0450 032.nt.4	35905	35905.03	Prostate2 array	2591-2650
DEX0450 032.nt.4	20237	20237.0	Breast array	1062-1121
DEX0450 032.nt.4	31591	31591.0	Breast array	1330-1389
DEX0450 032.nt.4	26953	26953.02	Prostate1 array	1521-1580
DEX0450 032.nt.4	15829	15829.0	Breast array	1668-1727
DEX0450 032.nt.4	15830	15830.0	Breast array	1638-1697
DEX0450 032.nt.4	31590	31590.0	Breast array	1521-1580
DEX0450 032.nt.4	16906	16906.0	Breast array	1332-1391
DEX0450 032.nt.4	35951	35951.01	Prostate2 array	1332-1391
DEX0450 032.nt.4	35901	35901.01	Prostate2 array	1328-1387
DEX0450 032.nt.5	35919	35919.02	Prostate2 array	4572-4631

DEX0450	032.nt.5	16111	16111.0	Breast array	4838-4897
DEX0450	032.nt.5	20237	20237.0	Breast array	1062-1121
DEX0450	032.nt.5	31256	31256.03	Prostate2 array	4024-4083
DEX0450	032.nt.5	35901	35901.01	Prostate2 array	4029-4088
DEX0450	032.nt.5	35957	35957.03	Prostate2 array	4838-4897
DEX0450	032.nt.5	15848	15848.0	Breast array	5762-5821
DEX0450	032.nt.5	15830	15830.0	Breast array	4339-4398
DEX0450	032.nt.5	15315	15315.0	Breast array	5282-5341
DEX0450	032.nt.5	26953	26953.02	Prostate1 array	4222-4281
DEX0450	032.nt.5	35955	35955.02	Prostate2 array	5762-5821
DEX0450	032.nt.5	35951	35951.01	Prostate2 array	4033-4092
DEX0450	032.nt.5	32036	32036.02	Prostate1 array	5762-5821
DEX0450	032.nt.5	15324	15324.0	Breast array	4572-4631
DEX0450	032.nt.5	19576	19576.0	Breast array	5762-5821
DEX0450	032.nt.5	34888	34888.0	Colon array	5785-5844
DEX0450	032.nt.5	15320	15320.0	Breast array	4029-4088
DEX0450	032.nt.5	32020	32020.02	Prostate1 array	1062-1121
DEX0450	032.nt.5	35959	35959.02	Prostate2 array	4838-4897
DEX0450	032.nt.5	16908	16908.0	Breast array	5762-5821
DEX0450	032.nt.5	35945	35945.03	Prostate2 array	5671-5730
DEX0450	032.nt.5	35897	35897.03	Prostate2 array	4369-4428
DEX0450	032.nt.5	31590	31590.0	Breast array	4222-4281
DEX0450	032.nt.5	15865	15865.0	Breast array	4024-4083
DEX0450	032.nt.5	15317	15317.0	Breast array	5495-5554
DEX0450	032.nt.5	31591	31591.0	Breast array	4031-4090
DEX0450	032.nt.5	16910	16910.0	Breast array	4838-4897
DEX0450	032.nt.5	35905	35905.03	Prostate2 array	5292-5351
DEX0450	032.nt.5	16912	16912.0	Breast array	5671-5730
DEX0450	032.nt.5	16906	16906.0	Breast array	4033-4092
DEX0450	032.nt.5	15829	15829.0	Breast array	4369-4428
DEX0450	032.nt.5	35907	35907.03	Prostate2 array	5671-5730
DEX0450	032.nt.6	16910	16910.0	Breast array	4838-4897
DEX0450	032.nt.6	31256	31256.03	Prostate2 array	4024-4083
DEX0450	032.nt.6	16908	16908.0	Breast array	5582-5641
DEX0450	032.nt.6	15324	15324.0	Breast array	4572-4631
DEX0450	032.nt.6	35901	35901.01	Prostate2 array	4029-4088
DEX0450	032.nt.6	15315	15315.0	Breast array	5282-5341
DEX0450	032.nt.6	35957	35957.03	Prostate2 array	4838-4897
DEX0450	032.nt.6	16912	16912.0	Breast array	5491-5550
DEX0450	032.nt.6	16111	16111.0	Breast array	4838-4897
DEX0450	032.nt.6	15865	15865.0	Breast array	4024-4083
DEX0450	032.nt.6	34888	34888.0	Colon array	5605-5664
DEX0450	032.nt.6	15320	15320.0	Breast array	4029-4088
DEX0450	032.nt.6	35919	35919.02	Prostate2 array	4572-4631
DEX0450	032.nt.6	26953	26953.02	Prostate1 array	4222-4281
DEX0450	032.nt.6	20237	20237.0	Breast array	1062-1121
DEX0450	032.nt.6	35897	35897.03	Prostate2 array	4369-4428
DEX0450	032.nt.6	35945	35945.03	Prostate2 array	5491-5550
DEX0450	032.nt.6	15829	15829.0	Breast array	4369-4428
DEX0450	032.nt.6	32036	32036.02	Prostate1 array	5582-5641
DEX0450	032.nt.6	35955	35955.02	Prostate2 array	5582-5641
DEX0450	032.nt.6	32020	32020.02	Prostate1 array	1062-1121
DEX0450	032.nt.6	15830	15830.0	Breast array	4339-4398
DEX0450	032.nt.6	35959	35959.02	Prostate2 array	4838-4897
DEX0450	032.nt.6	35905	35905.03	Prostate2 array	5292-5351
DEX0450	032.nt.6	35951	35951.01	Prostate2 array	4033-4092
DEX0450	032.nt.6	19576	19576.0	Breast array	5582-5641

DEX0450 032.nt.6	15848	15848.0	Breast array	5582-5641
DEX0450 032.nt.6	31591	31591.0	Breast array	4031-4090
DEX0450 032.nt.6	31590	31590.0	Breast array	4222-4281
DEX0450 032.nt.6	16906	16906.0	Breast array	4033-4092
DEX0450 032.nt.6	35907	35907.03	Prostate2 array	5491-5550
DEX0450 032.nt.7	32036	32036.02	Prostate1 array	5278-5337
DEX0450 032.nt.7	16912	16912.0	Breast array	5187-5246
DEX0450 032.nt.7	31591	31591.0	Breast array	4031-4090
DEX0450 032.nt.7	19576	19576.0	Breast array	5278-5337
DEX0450 032.nt.7	35919	35919.02	Prostate2 array	4323-4382
DEX0450 032.nt.7	15865	15865.0	Breast array	4024-4083
DEX0450 032.nt.7	35945	35945.03	Prostate2 array	5187-5246
DEX0450 032.nt.7	35907	35907.03	Prostate2 array	5187-5246
DEX0450 032.nt.7	31590	31590.0	Breast array	4222-4281
DEX0450 032.nt.7	15315	15315.0	Breast array	4798-4857
DEX0450 032.nt.7	15848	15848.0	Breast array	5278-5337
DEX0450 032.nt.7	35955	35955.02	Prostate2 array	5278-5337
DEX0450 032.nt.7	26953	26953.02	Prostate1 array	4222-4281
DEX0450 032.nt.7	15317	15317.0	Breast array	5011-5070
DEX0450 032.nt.7	15320	15320.0	Breast array	4029-4088
DEX0450 032.nt.7	32020	32020.02	Prostate1 array	1062-1121
DEX0450 032.nt.7	20237	20237.0	Breast array	1062-1121
DEX0450 032.nt.7	15324	15324.0	Breast array	4323-4382
DEX0450 032.nt.7	31256	31256.03	Prostate2 array	4024-4083
DEX0450 032.nt.7	35905	35905.03	Prostate2 array	4808-4867
DEX0450 032.nt.7	35901	35901.01	Prostate2 array	4029-4088
DEX0450 032.nt.7	16908	16908.0	Breast array	5278-5337
DEX0450 032.nt.7	35951	35951.01	Prostate2 array	4033-4092
DEX0450 032.nt.7	34888	34888.0	Colon array	5301-5360
DEX0450 032.nt.7	16906	16906.0	Breast array	4033-4092
DEX0450 033.nt.1	1234	1234.0	Lung array	528-587
DEX0450 033.nt.1	18480	18480.02	Ovarian array	528-587
DEX0450 033.nt.1	30532	30532.0	Colon array	526-585
DEX0450 033.nt.2	34642	34642.0	Colon array	1335-1394
DEX0450 033.nt.2	30532	30532.0	Colon array	525-584
DEX0450 033.nt.2	1234	1234.0	Lung array	527-586
DEX0450 033.nt.2	24954	24954.02	Prostate1 array	1306-1365
DEX0450 033.nt.2	34643	34643.0	Colon array	1295-1354
DEX0450 033.nt.2	18480	18480.02	Ovarian array	527-586
DEX0450 033.nt.2	5421	5421.0	Lung array	1233-1292
DEX0450 033.nt.2	28019	28019.02	Prostate1 array	1335-1394
DEX0450 034.nt.1	37498	37498.0	Colon array	409-468
DEX0450 035.nt.1	20153	20153.0	Colon array	1276-1335
DEX0450 035.nt.1	20154	20154.0	Colon array	1230-1289
DEX0450 036.nt.1	5961	5961.0	Lung array	1321-1380
DEX0450 036.nt.1	37616	37616.0	Colon array	1951-2010
DEX0450 036.nt.1	37635	37635.0	Colon array	1975-2034
DEX0450 036.nt.1	37615	37615.0	Colon array	1991-2050
DEX0450 037.nt.1	1022	1022.0	Lung array	480-539
DEX0450 037.nt.1	12335	12335.02	Ovarian array	374-433
DEX0450 037.nt.1	33741	33741.0	Colon array	408-467
DEX0450 037.nt.1	29069	29069.01	Prostate2 array	374-433
DEX0450 037.nt.1	1023	1023.0	Lung array	425-484
DEX0450 037.nt.1	36689	36689.01	Prostate1 array	547-606
DEX0450 037.nt.1	29065	29065.03	Prostate2 array	480-539
DEX0450 038.nt.1	38976	38976.0	Colon array	457-516
DEX0450 038.nt.1	38975	38975.0	Colon array	483-542

DEX0450	039.nt.1	38502	38502.0	Colon array	457-516
DEX0450	039.nt.1	38501	38501.0	Colon array	558-617
DEX0450	039.nt.2	38499	38499.0	Colon array	1002-1061
DEX0450	039.nt.2	36599	36599.0	Colon array	779-838
DEX0450	039.nt.2	38501	38501.0	Colon array	559-618
DEX0450	039.nt.2	38502	38502.0	Colon array	458-517
DEX0450	039.nt.2	38509	38509.0	Colon array	996-1055
DEX0450	039.nt.2	38510	38510.0	Colon array	799-858
DEX0450	039.nt.2	38428	38428.0	Colon array	1001-1060
DEX0450	039.nt.3	38499	38499.0	Colon array	878-937
DEX0450	039.nt.3	38510	38510.0	Colon array	675-734
DEX0450	039.nt.3	36599	36599.0	Colon array	655-714
DEX0450	039.nt.3	38509	38509.0	Colon array	872-931
DEX0450	039.nt.3	38428	38428.0	Colon array	877-936
DEX0450	039.nt.3	38501	38501.0	Colon array	435-494
DEX0450	039.nt.4	38510	38510.0	Colon array	1091-1150
DEX0450	039.nt.4	36599	36599.0	Colon array	1071-1130
DEX0450	039.nt.4	38501	38501.0	Colon array	793-852
DEX0450	039.nt.4	38502	38502.0	Colon array	692-751
DEX0450	039.nt.4	38428	38428.0	Colon array	1293-1352
DEX0450	039.nt.4	38509	38509.0	Colon array	1288-1347
DEX0450	039.nt.4	38499	38499.0	Colon array	1294-1353
DEX0450	039.nt.5	38501	38501.0	Colon array	793-852
DEX0450	039.nt.5	38502	38502.0	Colon array	692-751
DEX0450	039.nt.6	38501	38501.0	Colon array	793-852
DEX0450	040.nt.1	39582	39582.0	Colon array	545-604
DEX0450	040.nt.1	35521	35521.0	Colon array	498-557
DEX0450	040.nt.1	39581	39581.0	Colon array	655-714
DEX0450	040.nt.1	35520	35520.0	Colon array	655-714
DEX0450	041.nt.1	36756	36756.0	Colon array	110-169
DEX0450	041.nt.1	33072	33072.0	Colon array	470-529
DEX0450	041.nt.1	33075	33075.0	Colon array	979-1038
DEX0450	041.nt.1	29313	29313.03	Prostate2 array	1076-1135
DEX0450	041.nt.1	36755	36755.0	Colon array	130-189
DEX0450	041.nt.1	37290	37290.0	Colon array	1167-1226
DEX0450	041.nt.1	33074	33074.0	Colon array	1076-1135
DEX0450	041.nt.1	29311	29311.03	Prostate2 array	470-529
DEX0450	042.nt.1	33118	33118.0	Colon array	3762-3821
DEX0450	042.nt.1	40737	40737.0	Colon array	2151-2210
DEX0450	042.nt.1	34009	34009.0	Colon array	3065-3124
DEX0450	042.nt.1	33119	33119.0	Colon array	3722-3781
DEX0450	042.nt.2	33118	33118.0	Colon array	2347-2406
DEX0450	042.nt.2	34009	34009.0	Colon array	1650-1709
DEX0450	042.nt.2	33119	33119.0	Colon array	2307-2366
DEX0450	042.nt.2	40737	40737.0	Colon array	736-795
DEX0450	043.nt.1	35881	35881.0	Colon array	2681-2740
DEX0450	043.nt.1	36670	36670.0	Colon array	6794-6853
DEX0450	043.nt.1	35882	35882.0	Colon array	2641-2700
DEX0450	043.nt.1	36669	36669.0	Colon array	6919-6978
DEX0450	044.nt.1	24211	24211.0	Breast array	173-232
DEX0450	044.nt.1	9110	9110.0	Colon array	206-265
DEX0450	044.nt.1	24210	24210.0	Breast array	206-265
DEX0450	044.nt.2	9110	9110.0	Colon array	1624-1683
DEX0450	044.nt.2	24211	24211.0	Breast array	1591-1650
DEX0450	044.nt.2	24210	24210.0	Breast array	1624-1683
DEX0450	044.nt.3	9110	9110.0	Colon array	794-853
DEX0450	044.nt.3	24210	24210.0	Breast array	794-853

DEX0450	044.nt.3	24211	24211.0	Breast array	761-820
DEX0450	045.nt.1	5599	5599.0	Lung array	873-932
DEX0450	045.nt.1	19854	19854.0	Breast array	785-844
DEX0450	045.nt.1	13784	13784.0	Colon array	765-824
DEX0450	045.nt.1	19853	19853.0	Breast array	805-864
DEX0450	045.nt.1	13783	13783.0	Colon array	805-864
DEX0450	046.nt.1	10297	10297.0	Colon array	353-412
DEX0450	047.nt.1	38789	38789.0	Colon array	1517-1576
DEX0450	047.nt.1	30511	30511.0	Colon array	611-670
DEX0450	047.nt.1	39412	39412.0	Colon array	1515-1574
DEX0450	048.nt.1	41177	41177.0	Colon array	549-608
DEX0450	048.nt.1	41178	41178.0	Colon array	519-578
DEX0450	049.nt.1	31424	31424.0	Colon array	603-662
DEX0450	049.nt.1	31425	31425.0	Colon array	532-591
DEX0450	050.nt.1	9398	9398.0	Colon array	808-867
DEX0450	050.nt.1	9399	9399.0	Colon array	764-823
DEX0450	052.nt.1	37943	37943.0	Colon array	522-581
DEX0450	052.nt.1	37944	37944.0	Colon array	402-461
DEX0450	053.nt.1	9398	9398.0	Colon array	809-868
DEX0450	053.nt.1	9399	9399.0	Colon array	765-824
DEX0450	053.nt.1	31645	31645.0	Breast array	1875-1934
DEX0450	053.nt.1	31644	31644.0	Breast array	1945-2004

Example 2b: Relative Quantitation of Gene Expression

Real-Time quantitative PCR with fluorescent Taqman[®] probes is a quantitation detection system utilizing the 5'-3' nuclease activity of Taq DNA polymerase. The method uses an internal fluorescent oligonucleotide probe (Taqman[®]) labeled with a 5' reporter dye and a downstream, 3' quencher dye. During PCR, the 5'-3' nuclease activity of Taq DNA polymerase releases the reporter, whose fluorescence can then be detected by the laser detector of the Model 7700 Sequence Detection System (PE Applied Biosystems, Foster City, CA, USA). Amplification of an endogenous control is used to standardize the amount of sample RNA added to the reaction and normalize for Reverse Transcriptase (RT) efficiency. Either cyclophilin, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), ATPase, or 18S ribosomal RNA (rRNA) is used as this endogenous control. To calculate relative quantitation between all the samples studied, the target RNA levels for one sample were used as the basis for comparative results (calibrator). Quantitation relative to the "calibrator" can be obtained using the comparative method (User Bulletin #2: ABI PRISM 7700 Sequence Detection System).

The tissue distribution and the level of the target gene are evaluated for every sample in normal and cancer tissues. Total RNA is extracted from normal tissues, cancer tissues, and from cancers and the corresponding matched adjacent tissues. Subsequently, first strand cDNA is prepared with reverse transcriptase and the polymerase chain reaction

is done using primers and Taqman[®] probes specific to each target gene. The results are analyzed using the ABI PRISM 7700 Sequence Detector. The absolute numbers are relative levels of expression of the target gene in a particular tissue compared to the calibrator tissue.

5 One of ordinary skill can design appropriate primers. The relative levels of expression of the CSNA versus normal tissues and other cancer tissues can then be determined. All the values are compared to the calibrator. Normal RNA samples are commercially available pools, originated by pooling samples of a particular tissue from different individuals.

10 The relative levels of expression of the CSNA in pairs of matched samples may also be determined. A matched pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. All the values are compared to the calibrator.

In the analysis of matching samples, the CSNAs show a high degree of tissue specificity for the tissue of interest. These results confirm the tissue specificity results obtained with normal pooled samples. Further, the level of mRNA expression in cancer samples and the isogenic normal adjacent tissue from the same individual are compared. This comparison provides an indication of specificity for the cancer state (e.g. higher levels of mRNA expression in the cancer sample compared to the normal adjacent).

20 Information on the samples tested in the QPCR experiments below include the Sample ID (Smpl ID), Tissue, Tissue Type (Tiss Type), Diagnosis (DIAG), Disease Detail, and Stage or Grade (STG or GRD) in following table.

Sample ID	Tissue	TISS TYPE	DIAG	DISEASE DETAIL	STG or GRD
AS12	Colon	CAN		T	Stage B
AS12	Colon	NAT		NL	
AS46	Colon	CAN		malignant	T3N1MX
AS46	Colon	NAT		NAT	
B34	Colon	CAN	Adenocarcinoma		
B34	Colon	NAT		NAT	
C9XR	Colon	CAN		Rectum Cancer	Stage D
C9XR	Colon	NAT		NAT	
CM67	Colon	CAN	Adenocarcinoma	Adenocarcinoma of cecum, Moderately differentiated	Stage II
CM67	Colon	NAT		NAT	
TX89	Colon	CAN	Adenocarcinoma	Adenocarcinoma of Transverse Colon	Stage IV
TX89	Colon	NAT		NAT	

AS43	Colon	CAN	Adenocarcinoma	malignant	
AS43	Colon	NAT	Adenocarcinoma	NAT	
AS98	Colon	CAN	Adenocarcinoma	Moderately to poorly differentiated adenocarcinoma	Duke's C
AS98	Colon	NAT		NAT	
RS53	Colon	CAN	Adenocarcinoma	moderately differentiated adenocarcinoma	
RS53	Colon	NAT	Adenocarcinoma	NAT	
RC01	Colon	CAN	Cancer		Stage IV
RC01	Colon	NAT		NAT	
SG27	Colon	CAN		malig	Stage B
SG27	Colon	NAT		NAT	
DC19	Colon	CAN		T	Stage B
DC19	Colon	NAT		NL	
401C	Colon	CAN	Adenocarcinoma	Adenocarcinoma of ascending colon and cecum	Stage III
401C	Colon	NAT		NAT	
CM12	Colon	CAN		T	Stage D
CM12	Colon	NAT	Adenocarcinoma	Nat	
TX01	Colon	CAN	Adenocarcinoma	Moderately differentiated adenocarcinoma of cecum	Stage II; T3NoMo
TX01	Colon	NAT		NAT	
DC22	Colon	CAN		Cancer	
DC22	Colon	NAT		NAT	
030B	Urinary Bladder	CAN	Carcinoma	invasive Carcinoma, poorly differentiated	Stage III, Grade 3
030B	Urinary Bladder	NAT		NAT	
TR17	Urinary Bladder	CAN	Carcinoma	transitional cell carcinoma	Stage II/Grade III
TR17	Urinary Bladder	NAT		NAT	
520B	Urinary Bladder	CAN	Sarcomatoid transitional cell carcinoma	Sarcomatoid transitional cell carcinoma	
520B	Urinary Bladder	NAT		NAT	
KS52	Cervix	CAN	Squamous cell carcinoma	Keratinizing Squamous Cell Carcinoma	IIIB, well diff. G1; T3bNxM0
KS52	Cervix	NAT		NAT	
NK23	Cervix	CAN		Nonkeratinizing Large Cell	FIGO IIIB, undiff. G4; T3bNxM0
NK23	Cervix	NAT		NAT	
NKS54	Cervix	CAN	Squamous cell carcinoma	Nonkeratinizing Squamous Cell Carcinoma	IIB, mod diff. G2; T2bNxM0
NKS54	Cervix	NAT		NAT	

NKS55	Cervix	CAN	Squamous cell carcinoma	Nonkeratinizing Squamous Cell Carcinoma	IIIB, Mod diff. G2; T3bNxM0
NKS55	Cervix	NAT		NAT	
NKS81	Cervix	CAN	Squamous cell carcinoma	large cell nonkeratinizing sq carc, IIB, moderately diff	IIB
NKS81	Cervix	NAT		NAT	
NKS25	Cervix	CAN			
NKS25	Cervix	NAT		NAT	
NKS18	Cervix	CAN	Squamous cell carcinoma	Nonkeratinizing squamous cell carcinoma	GII
NKS18	Cervix	NAT		NAT	
10479	Endometrium	CAN		malignant mixed mullerian tumor	T?, Nx, M1
10479	Endometrium	NAT		NAT	
28XA	Endometrium	CAN	Endometrial adenocarcinoma	malignant	II/III
28XA	Endometrium	NAT		NAT	II/III
8XA	Endometrium	CAN	mod. diff, invasive, squamous differentiation, FIGO-II		
8XA	Endometrium	NAT		NAT	
106XD	Kidney	CAN	Renal cell carcinoma	renal cell carcinoma, clear cell, localized	3
106XD	Kidney	NAT		NL	
107XD	Kidney	CAN	Renal cell carcinoma	renal cell carcinoma, clear cell, with metastatic	G III
107XD	Kidney	NAT		NL	
109XD	Kidney	CAN		Malignant	G III
109XD	Kidney	NAT		NL	
10XD	Kidney	CAN	Renal cell carcinoma	renal cell carcinoma, clear cell, localized, grade 2-3	3
10XD	Kidney	NAT		NL	
22K	Kidney	CAN	Renal cell carcinoma	Renal cell carcinoma	G2, Mod. Diff.
22K	Kidney	NAT		NAT	
12XD	Kidney	CAN	Renal cell carcinoma	Left renal cell carcinoma	
12XD	Kidney	NAT		NAT	
15XA	Liver	CAN		Sarcoma, Retroperitoneal Tumor	Grade-2
15XA	Liver	NAT		CA	St. I, G4
174L	Liver	CAN	Hepatocellular carcinoma	Moderate to well differentiated hepatocellular carcinoma	

174L	Liver	NAT	Hepatocellular carcinoma	NAT	
187L	Liver	CAN	Adenocarcinoma	Metastatic Adenocarcinoma	Liver (Gallbladder)
187L	Liver	NAT		NAT	
205L	Lung	CAN	Adenocarcinoma	poorly differentiated adenocarcinoma	T2, N1, Mx
205L	Lung	NAT		NAT	
315L	Lung	CAN	Squamous cell carcinoma		
315L	Lung	NAT	Adenocarcinoma	NAT	
507L	Lung	CAN	Bronchioloalveolar carcinoma	bronchioalveolar carcinoma	Stage IB, G1, well diff.
507L	Lung	NAT		NAT	
528L	Lung	CAN	Adenocarcinoma	Adenocarcinoma	St.IV, T2N0M1, infiltrating poorly diff.
528L	Lung	NAT		NAT	
8837L	Lung	CAN	Squamous cell carcinoma	Squamous cell carcinoma	T2, N0, M0
8837L	Lung	NAT		NAT	
AC11	Lung	CAN	Adenocarcinoma	poorly differentiated adenocarcinoma	T2, N2, M1
AC11	Lung	NAT		NAT	
AC39	Lung	CAN	Adenocarcinoma	intermediate grade adnecarcinoma	T2, N2, Mx
AC39	Lung	NAT		NAT	
SQ80	Lung	CAN	Squamous cell carcinoma	poorly differentiated squamous cell carcinoma	T1, N1, M0
SQ80	Lung	NAT		NAT	
SQ81	Lung	CAN	Squamous cell carcinoma	poorly differentiated squamous carcinoma	T3, N1, Mx
SQ81	Lung	NAT		NAT	
19DN	Mammary	CAN	Invasive ductal carcinoma	Invasive ductal carcinoma	G3, Stage IIA; T2N0M0
19DN	Mammary	NAT		NAT	
42DN	Mammary	CAN	Invasive ductal carcinoma	Invasive Ductal Carcinoma	T3aN1M0 IIIA, G3
42DN	Mammary	NAT		NAT	
517	Mammary	CAN	Infiltrating ductal carcinoma	Infiltrating ductal carcinoma	St. IIA, G3
517	Mammary	NAT		NAT	

781M	Mammary	CAN	Invasive ductal carcinoma		Architectural grade-3/3, Nuclear grade-3/3
781M	Mammary	NAT		NAT	
869M	Mammary	CAN	Invasive carcinoma	Invasive Carcinoma	Stage IIA G1; T2N0Mo
869M	Mammary	NAT		NAT	
976M	Mammary	CAN	Invasive ductal carcinoma	Invasive Ductal Carcinoma	T2N1M0 (Stage 2B Grade 2-3)
976M	Mammary	NAT		NAT	
S570	Mammary	CAN	Carcinoma	Carcinoma	Stage IIA; T1N1Mo
S570	Mammary	NAT		NAT	
S699	Mammary	CAN	Invasive lobular carcinoma	Invasive Lobular Carcinoma	Stage IIB G1; T2N1Mo
S699	Mammary	NAT		NAT	
S997	Mammary	CAN	Invasive ductal carcinoma	Invasive Ductal Carcinoma	Stage IIB G3; T2N1Mo
S997	Mammary	NAT		NAT	
G021	Ovary	CAN	Carcinoma	St. IIIC, poorly diff.	Stage- IIIC, poorly diff.
G021	Ovary	NAT		NAT	
10050	Ovary	CAN		papillary serous and endometrioid ovarian carcinoma, concurrent metastatic breast cancer	3
10400	Ovary	CAN		papillary serous adeno, metastatic	
1050	Ovary	CAN		Papillary Serous Carcinoma with Focal Mucinous Differentiation	Stage IC G0; T1cN0M0
130X	Ovary	CAN		Ovarian cancer	
7180	Ovary	CAN	Adenocarcinoma	malignant tumor	IIIC
A1B	Ovary	CAN	Adenocarcinoma	CA	
1230	Ovary	NRM		Normal	
18GA	Ovary	NRM		NL	
206I	Ovary	NRM		NL	
3370	Ovary	NRM		Normal	
40G	Ovary	NRM		NL	
5150	Ovary	NRM		Normal	
C004	Ovary	NRM		NL	
C177	Ovary	NRM		several fluid filled cysts	
4510	Ovary	NRM		Normal Tissue	
7180	Ovary	CAN	Adenocarcinoma	malignant tumor	IIIC
71XL	Pancreas	CAN		villous adenoma with paneth cell metaplasia	localized

71XL	Pancreas	NAT		NL	
82XP	Pancreas	CAN		serious cystadenoma	
82XP	Pancreas	NAT		NL	
92X	Pancreas	CAN	Ductal adenocarcinoma	ductal adenocarcinoma	mod to focally poorly diff.
92X	Pancreas	NAT		NL	
77X	Pancreas	CAN	Hepatic adenoma	Hepatic adenoma	
77X	Pancreas	NAT		NL	
23B	Prostate	CAN		Prostate tumor	Gleason's 3+4
23B	Prostate	NAT		NAT	
65XB	Prostate	CAN	Adenocarcinoma	adenocarcinom	3+4=7
65XB	Prostate	NAT		NL	
675P	Prostate	CAN	Adenocarcinoma	adenocarcinoma	
675P	Prostate	NAT		Normal	
84XB	Prostate	CAN	Adenocarcinoma	adenocarcinom	2+3
84XB	Prostate	NAT		NL	
958P	Prostate	CAN	Adenocarcinoma	Adenocarcinoma	T2C, NO, MX
958P	Prostate	NAT	NAT	Normal	
263C	Prostate	BPH		BPH	
276P	Prostate	BPH		BPH	
767B	Prostate	BPH		prostate BPH	
855P	Prostate	BPH		BPH	
10R	Prostate	PROST		active chronic prostatitis	T0, N0, M0
20R	Prostate	PROST		PROSTATITIS	
287S	Skin	CAN	Squamous cell carcinoma	Invasive Keratinizing Squamous Cell Carcinoma	Moderately Differentiated
287S	Skin	NAT		NAT	
39A	Skin	CAN		CA	St. II
39A	Skin	NAT		CA	St. II
669S	Skin	CAN	Melanoma	Nodular malignant melanoma	
669S	Skin	NAT		NAT	

171S	Small Intestine	CAN	Adenocarcinoma	Moderately differentiated Adenocarcinoma, invasive	
171S	Small Intestine	NAT		NAT	
20SM	Small Intestine	CAN	Adenocarcinoma	Adenocarcinoma, metastatic to lung & liver	St. IV, poorly diff.
20SM	Small Intestine	NAT		NAT	
H89	Small Intestine	CAN	Adenocarcinoma	Adenocarcinoma	80% tumor, 50% necrosis, moderately differentiated, G2-3; T3N1MX
H89	Small Intestine	NAT	Adenocarcinoma	NAT	
261S	Stomach	CAN	Signet-ring cell carcinoma	Signet-ring cell carcinoma	Stage IIIA, T3N1M0
261S	Stomach	NAT		NAT	
288S	Stomach	CAN	Adenocarcinoma	Infiltrating Adenocarcinoma	Moderately Differentiated
288S	Stomach	NAT		NAT	
AC93 or 509L	Stomach	CAN	Adenocarcinoma	Adenocarcinoma	St. IV, G4, T4N3M0, poorly diff.
AC93 or 509L	Stomach	NAT		NAT	
88S	Stomach	CAN	Adenocarcinoma	Mucinous adenocarcinoma	T3N1M0, St. IIIA
88S	Stomach	NAT		NAT	
143N	Thyroid Gland	CAN	Follicular carcinoma	Follicular Carcinoma	
143N	Thyroid Gland	NAT		NAT	
270T	Thyroid Gland	CAN		CA	
270T	Thyroid Gland	NAT		NAT	
56T	Thyroid Gland	CAN	Papillary carcinoma	Papillary Carcinoma	St. III; T4N1M0
56T	Thyroid Gland	NAT		NAT	
39X	Testes	CAN		CA	
39X	Testes	NAT		NAT	
647T	Testes	CAN	Teratocarcinoma	Teratocarcinoma	Stage IA
647T	Testes	NAT	Teratocarcinoma	NAT	

663T	Testes	CAN	Teratocarcinoma	Teratocarcinoma	
663T	Testes	NAT		NAT	
135XO	Uterus	CAN		Uterus normal	
135XO	Uterus	NAT		Uterus tumor	
85XU	Uterus	CAN		endometrial carcinoma	I
85XU	Uterus	NAT		NL	
B1	Blood	NRM		Normal	
B3	Blood	NRM		Normal	
B5	Blood	NRM		Normal	
B6	Blood	NRM		Normal	
B11	Blood	NRM		Normal	
982B	Blood	NRM		Normal	
B69	Blood	NRM		Normal	
B72	Blood	NRM		Normal	
B73	Blood	NRM		Normal	
B75	Blood	NRM		Normal	
48AD	Adrenal Gland	NRM		Normal	
10BR	Brain	NRM		Normal	
01CL	Colon	NRM		Normal	
06CV	Cervix	NRM		Normal	
01ES	Esophagus	NRM		Normal	
46HR	Heart	NRM		Normal	
00HR	Human Reference	CAN	CAN	Cancer pool	
55KD	Kidney	NRM		Normal	
89LV	Liver	NRM		Normal	
90LN	Lung	NRM		Normal	
01MA	Mammary	NRM		Normal	
84MU	Skeletal Muscle	NRM		Normal	
3APV	Ovary	NRM		Normal	
04PA	Pancreas	NRM		Normal	
59PL	Placenta	NRM		Normal	
09PR	Prostate	NRM		Normal	
21RC	Rectum	NRM		Normal	
59SM	Small Intestine	NRM		Normal	
7GSP	Spleen	NRM		Normal	
09ST	Stomach	NRM		Normal	
4GTS	Testes	NRM		Normal	
99TM	Thymus Gland	NRM		Normal	
16TR	Trachea	NRM		Normal	
57UT	Uterus	NRM		Normal	

The relative expression level of Cln260 in various tissue samples is included below. Tissue samples include 78 pairs of matching samples, 7 non matched cancer samples, and 34 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the

5 normal adjacent sample for that same tissue from the same individual. Of the normal samples 4 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to colon cancer sample CLNC9XR (calibrator).

The table below contains the relative expression level values for the sample as

10 compared to the calibrator. The table includes the Sample ID and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
CLNAS12	0.28	0.60			
CLNAS46	1.08	0.07			
CLNB34	0.52	0.00			
CLNC9XR	1.00	0.36			
CLNCM67	0.99	0.78			
CLNTX89	1.14	1.87			
CLNAS43	0.00	0.00			
CLNAS98	0.00	0.00			
CLNRS53	4.88	6.41			
CLNRC01	5.96	1.53			
CLNSG27	0.00	1.92			
CLNDC19	6.28	0.00			
CLN401C	4.67	4.98			
CLNCM12	1.29	0.00			
CLNTX01	3.99	0.00			
BLD030B	0.90	0.00			
BLD520B	0.00	0.67			
BLDTR17	0.00	0.79			
CVXKS52	0.00	1.28			
CVXNK23	0.73	0.00			
CVXNKS54	0.00	0.00			
CVXNKS55	0.00	0.00			
CVXNKS81	0.00	0.00			
ENDO10479	0.00	6.68			
ENDO28XA	0.00	2.17			
ENDO8XA	0.00	0.16			
KID106XD	0.00	0.00			
KID107XD	4.62	0.00			
KID109XD	1.15	0.00			

KID10XD	6.52	0.00			
KID22K	0.11	0.12			
LNG205L	0.00	0.00			
LNG315L	5.00	0.00			
LNG507L	0.00	0.00			
LNG528L	0.00	0.00			
LNG8837L	1.78	1.31			
LNGAC11	0.32	0.00			
LNGAC39	0.00	0.00			
LNGSQ80	0.00	0.00			
LNGSQ81	0.00	3.36			
LVR15XA	0.60	0.36			
LVR174L	0.00	1.25			
LVR187L	0.00	1.21			
MAM19DN	0.00	0.00			
MAM42DN	0.00	0.00			
MAM517	0.00	0.00			
MAM781M	0.00	0.00			
MAM869M	2.67	0.00			
MAM976M	0.00	0.00			
MAMS570	0.00	0.00			
MAMS699	7.10	0.00			
MAMS997	0.00	0.00			
OVRG021	0.00	0.00			
OVR10050	0.00				
OVR10400	0.56				
OVR1050	3.85				
OVR130X	0.00				
OVR7180	0.00				
OVR1A1B	0.95				
OVR1230			0.00		
OVR18GA			2.81		
OVR206I			0.00		
OVR3370			0.00		
OVR40G			2.37		
OVR5150			0.00		
OVR004			0.00		
OVR177			0.00		
PAN71XL	0.00	0.00			
PAN82XP	2.06	0.00			
PAN92X	0.00	0.00			
PRO23B	0.00	0.00			
PRO65XB	0.00	0.49			
PRO675P	0.00	0.00			
PRO84XB	0.00	0.00			
PRO958P	0.61	5.74			
PRO263C				0.00	

PRO276P				0.00	
PRO767B				0.00	
PRO855P				1.29	
PRO10R					0.00
PRO20R					0.00
SKN287S	0.00	0.00			
SKN39A	0.00	0.00			
SKN669S	0.00	0.00			
SMINT171S	0.00	0.00			
SMINT20SM	0.00	0.00			
SMINTH89	0.00	0.00			
STO261S	0.00	0.00			
STO288S	1.05	0.00			
STO88S	0.00	0.00			
THRD143N	2.72	0.00			
THRD270T	0.00	0.00			
THRD56T	0.00	0.00			
TST39X	0.00	0.00			
TST647T	0.00	1.74			
TST663T	3.23	4.68			
UTR135XO	0.00	0.00			
UTR85XU	26.65	1.06			
BLOB3			0.00		
BLOB6			0.00		
BLOB11			0.00		
BLO982B			0.00		
ADR48AD			0.00		
HUMREF00HR	0.00				
BRN10BR			0.00		
CLN01CL			0.87		
ESO01ES			0.00		
HRT46HR			0.00		
KID55KD			0.32		
LVR89LV			0.00		
LNG90LN			1.06		
MAM01MA			0.00		
MSL84MU			0.00		
OVR3APV			0.14		
PAN04PA			0.54		
PLA59PL			0.00		
PRO09PR			1.53		
REC21RC			0.00		
SMINT59SM			0.95		
SPL7GSP			1.36		
STO09ST			0.00		
THYM99TM			0.00		
TRA16TR			0.00		

TST4GTS			7.07		
UTR57UT			2.99		

0.00= Negative or Not Detected

The sensitivity for Cln260 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Cln260 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of colon tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Cln260 being useful as a colon cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	47%	22%	22%	0%	0%
Sensitivity, Down vs. NAT	13%	11%	0%	0%	40%
Sensitivity, Up vs. NRM	33%	11%	22%	43%	0%
Sensitivity, Down vs. NRM	27%	78%	0%	0%	100%
Specificity	70.93%	64.13%	61.96%	64.52%	63.98%

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Cln260 a good marker for diagnosing, monitoring, staging, imaging and/or treating colon cancer.

Additionally, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Cln260 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Cln260 are as follows:

(Cln260_forward): GGCCAACTCTTTTACTCCTTCATT (SEQ ID NO:249)

(Cln260_reverse): CAGGAGCATCTCCGTTTTCATT (SEQ ID NO:250)

(Cln260_probe): TCCAGTAGTTGGGAGTGCTGGCA (SEQ ID NO:251)

DEX0450_053.nt.1 (Cln261)

The relative expression level of Cln261 in various tissue samples is included below.

Tissue samples include 78 pairs of matching samples, 8 non matched cancer samples, and 36 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to normal breast sample Mam01MA (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
CLNAS12	1.30	0.14			
CLNAS46	0.55	0.69			
CLNB34	0.89	0.00			
CLNCM67	1.18	0.14			
CLNDC22	0.31	3.01			
CLNTX89	0.81	0.21			
CLN401C	0.65	0.38			
CLNAS43	1.56	0.72			
CLNAS98	0.14	0.19			
CLNCM12	0.34	0.06			
CLNDC19	0.89	0.40			
CLNRC01	1.54	0.28			
CLNRS53	2.47	1.29			
CLNSG27	1.62	0.27			
CLNTX01	0.85	0.85			
BLD030B	2.56	1.55			
BLD520B	0.48	1.04			
BLDTR17	1.50	0.71			
CVXKS52	1.87	0.34			
CVXNKS55	1.11	1.04			
CVXNKS25	2.45	2.61			
CVXNKS18	0.06	0.32			
CVXNKS54	2.53	1.33			
ENDO10479	16.57	2.34			
ENDO28XA	3.15	1.37			
ENDO8XA	0.32	2.21			
KID106XD	0.09	0.10			
KID12XD	0.14	1.54			

KID10XD	0.11	0.04			
KID22K	0.23	0.14			
KID107XD	0.42	0.18			
LNG205L	2.84	0.22			
LNG315L	2.27	1.88			
LNG507L	1.74	0.99			
LNG528L	7.04	2.07			
LNG8837L	4.48	0.98			
LNGAC11	1.78	1.93			
LNGAC39	11.41	2.38			
LNGSQ80	3.11	1.94			
LNGSQ81	4.22	3.14			
LVR15XA	0.16	0.06			
LVR174L	0.01	0.05			
LVR187L	0.06	0.50			
MAM19DN	0.90	0.42			
MAM42DN	1.21	0.65			
MAM517	0.99	0.07			
MAM781M	0.67	0.29			
MAM869M	0.62	0.13			
MAM976M	0.33	0.39			
MAMS570	0.08	0.86			
MAMS699	0.66	0.88			
MAMS997	3.12	1.05			
OVRG021	0.71	3.06			
OVR206I			1.06		
OVR515O			0.52		
OVR18GA			0.73		
OVR337O			0.65		
OVR123O			0.00		
OVR177			0.57		
OVR40G			1.11		
OVR1005O	0.61				
OVR1040O	4.19				
OVR105O	0.53				
OVR130X	3.60				
OVR451O			0.90		
OVR718O	1.88				
OVR1B	3.31				
PAN71XL	0.40	0.40			
PAN77X	0.09				
PAN92X	0.21	0.71			
PRO10R					3.68
PRO20R					2.16
PRO23B	0.07	0.12			
PRO263C				1.40	
PRO276P				0.08	

PRO65XB	0.03	0.07			
PRO675P	0.13	0.09			
PRO767B				1.33	
PRO84XB	0.10	0.31			
PRO855P				0.05	
PRO958P	0.09	0.06			
SKN287S	0.27	0.21			
SKN39A	0.24	0.16			
SKN669S	0.45	0.10			
SMINT171S	0.16	0.08			
SMINT20SM	0.16	0.11			
SMINTH89	0.60	0.17			
STO261S	0.27	0.24			
STO288S	0.30	0.11			
STOAC93	0.26	0.50			
STO88S	0.29	0.03			
THRD143N	9.86	4.19			
THRD270T	3.59	2.98			
THRD56T	0.29	0.20			
TST39X	12.51	9.60			
TST647T	17.27	3.65			
TST663T	13.34	5.10			
UTR135XO	7.21	5.38			
UTR85XU	19.32	8.35			
BLOB3			0.02		
BLOB11			0.53		
BLO69			0.13		
BLO72			0.19		
BLO73			0.43		
ADR48AD			0.06		
BRN10BR			0.33		
CLN01CL			0.14		
CVX06CV			1.28		
ESO01ES			2.01		
HRT46HR			0.66		
HUMREF00HR	2.61				
KID55KD			0.48		
LVR89LV			0.05		
LNG90LN			14.3 5		
MAM01MA			1.00		
MSL84MU			1.62		
OVR3APV			4.73		
PAN04PA			0.23		
PLA59PL			1.23		
PRO09PR			1.09		
REC21RC			0.22		

251

SMINT59SM			0.15		
SPL7GSP			1.74		
STO09ST			0.33		
THYM99TM			0.54		
TRA16TR			0.97		
TST4GTS			2.46		
UTR57UT			1.28		

0.00= Negative or Not Detected

The sensitivity for Cln261 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Cln261 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of colon tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Cln261 being useful as a colon cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	60%	44%	56%	0%	0%
Sensitivity, Down vs. NAT	7%	0%	11%	0%	40%
Sensitivity, Up vs. NRM	93%	0%	11%	57%	0%
Sensitivity, Down vs. NRM	0%	89%	22%	0%	100%
Specificity	12.57%	37.43%	8.56%	25.93%	1.06%

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Cln261 a good marker for diagnosing, monitoring, staging, imaging and treating colon cancer.

Primers used for QPCR Expression Analysis of Cln261 are as follows:

(Cln261_forward): TCGGCAGACATGTGCATTG (SEQ ID NO:252)

(Cln261_reverse): CGTTGCTTGTACGCTCCGTAA (SEQ ID NO:253)

(Cln261_probe): CATTGCGATTCTCTTCTCATGATCCTGATATG (SEQ ID NO:254)

Conclusions

Altogether, the high level of tissue specificity, plus the mRNA overexpression in matched samples tested are indicative of SEQ ID NO: 1-94 being a diagnostic marker and/or a therapeutic target for cancer.

Example 3: Protein Expression

5 The CSNA is amplified by polymerase chain reaction (PCR) and the amplified DNA fragment encoding the CSNA is subcloned in pET-21d for expression in *E. coli*. In addition to the CSNA coding sequence, codons for two amino acids, Met-Ala, flanking the NH₂-terminus of the coding sequence of CSNA, and six histidines, flanking the COOH-terminus of the coding sequence of CSNA, are incorporated to serve as initiating
10 Met/restriction site and purification tag, respectively.

An over-expressed protein band of the appropriate molecular weight may be observed on a Coomassie blue stained polyacrylamide gel. This protein band is confirmed by Western blot analysis using monoclonal antibody against 6X Histidine tag.

15 Large-scale purification of CSP is achieved using cell paste generated from 6-liter bacterial cultures, and purified using immobilized metal affinity chromatography (IMAC). Soluble fractions that are separated from total cell lysate were incubated with a nickel chelating resin. The column is packed and washed with five column volumes of wash buffer. CSP is eluted stepwise with various concentration imidazole buffers.

Example 4: Fusion Proteins

20 The human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector. For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note
25 that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 2, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced. If the naturally occurring signal sequence is used to
30 produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. *See, e.g.,* WO 96/34891.

Example 5: Production of an Antibody from a Polypeptide

In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in any suitable tissue culture medium; however, it is preferable to
5 culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100, µg/ml of streptomycin. The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention;
10 however, it is preferable to employ the parent myeloma cell line (SP20), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands *et al.*, *Gastroenterology* 80: 225-232 (1981).

The hybridoma cells obtained through such a selection are then assayed to identify
15 clones which secrete antibodies capable of binding the polypeptide. Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific
20 antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein specific antibody and can be used to immunize an animal to
25 induce formation of further protein-specific antibodies.

Example 6: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA is isolated from individual patients or from a family of individuals that have a phenotype of interest. cDNA is then generated from these RNA samples using protocols
30 known in the art. *See*, Sambrook (2001), *supra*. The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO: 1-94. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C;

and 60-120 seconds at 70°C, using buffer solutions described in Sidransky *et al.*, *Science* 252(5006): 706-9 (1991). *See also* Sidransky *et al.*, *Science* 278(5340): 1054-9 (1997).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The
5 intron-exon borders of selected exons are also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations are then cloned and sequenced to validate the results of the direct sequencing. PCR products is cloned into T-tailed vectors as described in Holton *et al.*, *Nucleic Acids Res.*, 19: 1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected
10 individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements may also be determined. Genomic clones are nick-translated with digoxigenin deoxyuridine 5' triphosphate (Boehringer Mannheim), and FISH is performed as described in Johnson *et al.*, *Methods Cell Biol.* 35: 73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1
15 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C-and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and
20 variable excitation wavelength filters. Johnson (1991). Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

25 **Example 7: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample**

Antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal
30 and are produced by the method described above. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced. The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial

dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbound polypeptide. Next, 50 μ l of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three
5 times with deionized or distilled water to remove unbound conjugate. 75 μ l of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution are added to each well and incubated 1 hour at room temperature.

The reaction is measured by a microtiter plate reader. A standard curve is prepared, using serial dilutions of a control sample, and polypeptide concentrations are
10 plotted on the X-axis (log scale) and fluorescence or absorbance on the Y-axis (linear scale). The concentration of the polypeptide in the sample is calculated using the standard curve.

Example 8: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion
15 consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

20 As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1, μ g/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given
25 continuously, the secreted polypeptide is typically administered at a dose rate of about 1 μ g/kg/hour to about 50 mg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the
30 desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally,

topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which
5 include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semipermeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules. Sustained-
10 release matrices include polylactides (U. S. Pat. No.3,773,919, EP 58,481, the contents of which are hereby incorporated by reference herein in their entirety), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22: 547-556 (1983)), poly (2-hydroxyethyl methacrylate) (R. Langer et al., J. Biomed. Mater. Res. 15: 167-277 (1981), and R. Langer, Chem. Tech. 12: 98-105 (1982)), ethylene vinyl acetate
15 (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE Epstein et al., Proc. Natl. Acad. Sci. USA 82: 3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA 77: 4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese
20 Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324, the contents of which are hereby incorporated by reference herein in their entirety. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

25 For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation.

30 For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides. Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is

shaped into the desired formulation. Preferably, the carrier is a parenteral carrier, more preferably, a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as

5 liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic

10 acid; low molecular weight (less than about ten residues) polypeptides, e. g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such

15 as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers

20 will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a

25 stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1 % (w/v) aqueous polypeptide solution, and the resulting mixture

30 is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions

of the invention. Associated with such container (s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may
5 be employed in conjunction with other therapeutic compounds.

Example 9: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form.
10 Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose
15 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided above.

Example 10: Method of Treating Increased Levels of the Polypeptide

Antisense or RNAi technology are used to inhibit production of a polypeptide of
20 the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the
25 treatment was well tolerated. The formulation of the antisense polynucleotide is provided above.

Example 11: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a
30 subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a

tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e. g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks. pMV-7 (Kirschmeier, P. T. et al., DNA, 7: 219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 3. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB 101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+aml2 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media.

If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

5 The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

Example 12: Method of Treatment Using Gene Therapy-In Vivo

Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the
10 introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide.

The polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in
15 the art, see, for example, Tabata H. *et al. Cardiovasc. Res.* 35 (3): 470-479 (1997); Chao J *et al. Pharmacol. Res.* 35 (6): 517-522 (1997); Wolff J. A. *Neuromuscul. Disord.* 7 (5): 314-318 (1997), Schwartz B. *et al. Gene Ther.* 3 (5): 405-411 (1996); and Tsurumi Y. *et al. Circulation* 94 (12): 3281-3290 (1996); W0 90/11092, W0 98/11779; U. S. Patent No. 5,693,622; 5,705,151; 5,580,859, the contents of which are hereby incorporated by
20 reference herein in their entirety.

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, colon, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

25 The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P. L. *et al. Ann. NY*
30 *Acad. Sci.* 772: 126-139 (1995) and Abdallah B. *et al. Biol. Cell* 85 (1): 1-7 (1995)) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, colon, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 $\mu\text{g/kg}$ body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also

be used, such as, inhalation of an aerosol formulation particularly for delivery to colons or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

5 The dose response effects of injected polynucleotide in muscle in vivo is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps
10 muscles of mice are then injected with various amounts of the template DNA.

 Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute,
15 approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

 After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 μ m cross-section of the individual
20 quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice.

25 The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

Example 13: Transgenic Animals

 The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea
30 pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e. g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific

embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (I. e., polynucleotides of the invention) into animals to produce the founder lines of transgenic
5 animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., *Appl. Microbiol. Biotechnol.* 40: 691-698 (1994); Carver et al., *Biotechnology* 11: 1263-1270 (1993); Wright et al., *Biotechnology* 9: 830-834 (1991); and U. S. Pat. No. 4,873,191, the contents of which is hereby incorporated by reference herein in its entirety); retrovirus mediated gene transfer into germ lines (Van der Putten et al.,
10 *Proc. Natl. Acad. Sci., USA* 82: 6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., *Cell* 56: 313-321 (1989)); electroporation of cells or embryos (Lo, 1983, *Mol Cell. Biol.* 3: 1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e. g., Ulmer et al., *Science* 259: 1745 (1993); introducing nucleic acid constructs into embryonic pluripotent stem cells
15 and transferring the stem cells back into the blastocyst; and sperm mediated gene transfer (Lavitrano et al., *Cell* 57: 717-723 (1989). For a review of such techniques, see Gordon, "Transgenic Animals," *Intl. Rev. Cytol.* 115: 171-229 (1989).

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated
20 oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campbell et al., *Nature* 380: 64-66 (1996); Wilmut et al., *Nature* 385: 810813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, I. e., mosaic animals or chimeric. The transgene may be integrated as a single transgene
25 or as multiple copies such as in concatamers, e.g., head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., *Proc. Natl. Acad. Sci. USA* 89: 6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest,
30 and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of

integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., *Science* 265: 103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 14: Knock-Out Animals

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (E. g., see Smithies et al., *Nature* 317: 230-234 (1985); Thomas & Capecchi, *Cell* 51: 503512 (1987); Thompson et al., *Cell* 5: 313-321 (1989)) Alternatively, RNAi technology may be used. For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (e. g., see Thomas & Capecchi 1987 and Thompson 1989, *supra*). However, this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e. g., knockouts) are administered to a patient in vivo. Such cells may be obtained from the patient (i.e., animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e. g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc.

The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be
5 introduced into the patient systemically, e. g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, e. g., genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U. S. Patent No. 5,399,349; and
10 Mulligan & Wilson, U. S. Patent No. 5,460,959, the contents of which are hereby incorporated by reference herein in their entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the
15 cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of
20 polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

While preferred illustrative embodiments of the present invention are described, one skilled in the art will appreciate that the present invention can be practiced by other
25 than the described embodiments, which are presented for purposes of illustration only and not by way of limitation. The present invention is limited only by the claims that follow.

We claim:

1. An isolated nucleic acid molecule comprising:
 - (a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 95-248;
 - 5 (b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-94;
 - (c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b); or
 - (d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b).
- 10 2. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is a cDNA.
- 15 3. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is genomic DNA.
4. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is an RNA.
- 20 5. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is a mammalian nucleic acid molecule.
6. The nucleic acid molecule according to claim 5, wherein the nucleic acid molecule is a human nucleic acid molecule.
- 25 7. A method for determining the presence of a colon specific nucleic acid (CSNA) in a sample, comprising the steps of:
 - (a) contacting the sample with the nucleic acid molecule of SEQ ID NO: 1-94 under conditions in which the nucleic acid molecule will selectively hybridize to a colon specific nucleic acid; and
 - 30

(b) detecting hybridization of the nucleic acid molecule to a CSNA in the sample, wherein the detection of the hybridization indicates the presence of a CSNA in the sample.

- 5 8. A vector comprising the nucleic acid molecule of claim 1.
9. A host cell comprising the vector according to claim 8.
10. A method for producing a polypeptide encoded by the nucleic acid molecule
10 according to claim 1, comprising the steps of:
- (a) providing a host cell comprising the nucleic acid molecule operably linked
 to one or more expression control sequences, and
- (b) incubating the host cell under conditions in which the polypeptide is
 produced.
- 15
11. A polypeptide encoded by the nucleic acid molecule according to claim 1.
12. An isolated polypeptide selected from the group consisting of:
- (a) a polypeptide comprising an amino acid sequence with at least 95%
20 sequence identity to of SEQ ID NO: 95-248 ; or
- (b) a polypeptide comprising an amino acid sequence encoded by a nucleic
 acid molecule having at least 95% sequence identity to a nucleic acid molecule
 comprising a nucleic acid sequence of SEQ ID NO: 1-94.
- 25 13. An antibody or fragment thereof that specifically binds to:
- (a) a polypeptide comprising an amino acid sequence with at least 95%
 sequence identity to of SEQ ID NO: 95-248 ; or
- (b) a polypeptide comprising an amino acid sequence encoded by a nucleic
 acid molecule having at least 95% sequence identity to a nucleic acid molecule
30 comprising a nucleic acid sequence of SEQ ID NO: 1-94.
14. A method for determining the presence of a colon specific protein in a sample,
 comprising the steps of:

- (a) contacting the sample with a suitable reagent under conditions in which the reagent will selectively interact with the colon specific protein comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 95-248; and
- 5 (b) detecting the interaction of the reagent with a colon specific protein in the sample, wherein the detection of binding indicates the presence of a colon specific protein in the sample.
15. A method for diagnosing or monitoring the presence and metastases of colon
- 10 cancer in a patient, comprising the steps of:
- (a) determining an amount of:
- (i) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 95-248;
- (ii) a nucleic acid molecule comprising a nucleic acid sequence of SEQ
- 15 ID NO: 1-94;
- (iii) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (i) or (ii);
- (iv) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (i) or (ii);
- 20 (v) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 95-248 ; or
- (vi) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-94
- 25 and;
- (b) comparing the amount of the determined nucleic acid molecule or the polypeptide in the sample of the patient to the amount of the colon specific marker in a normal control; wherein a difference in the amount of the nucleic acid molecule or the polypeptide in the sample compared to the amount of the nucleic acid molecule or the polypeptide in the normal control is associated with the
- 30 presence of colon cancer.

16. A kit for detecting a risk of cancer or presence of cancer in a patient, said kit comprising a means for determining the presence of:

- (a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 95-248;
- 5 (b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-94;
- (c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b); or
- (d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b); or
- 10 (e) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 95-248 ; or
- (f) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-94.
- 15

17. A method of treating a patient with colon cancer, comprising the step of administering a composition consisting of:

- (a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 95-248;
- 20 (b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-94;
- (c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b);
- 25 (d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b);
- (e) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 95-248 ; or
- (f) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-94;
- 30

to a patient in need thereof, wherein said administration induces an immune response against the colon cancer cell expressing the nucleic acid molecule or polypeptide.

271

10/538002

JC17 Rec'd PCT/PTO 03 JUN 2005

18. A vaccine comprising the polypeptide or the nucleic acid encoding the polypeptide of claim 12.

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SEQUENCE LISTING

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<110> diaDexus, Inc.
Macina, Roberto
Turner, Leah
Sun, Yongming
Rodriguez, Maria
Tim Burcham

<120> Compositions, Splice Variants and Methods Relating to Colon
Specific Genes and Proteins

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<211> 2655

<212> DNA

<213> Homo sapien

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<211> 2570

<212> DNA

<213> Homo sapien

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<212> DNA
<213> Homo sapien

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<212> DNA

<213> Homo sapien

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<212> DNA
<213> Homo sapien

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<212> DNA
<213> Homo sapien

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 <213> Homo sapien

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<211> 1560

<212> DNA

<213> Homo sapien

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<212> DNA
<213> Homo sapien

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<212> DNA
<213> Homo sapien

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<210> 48
 <211> 2994
 <212> DNA
 <213> Homo sapien

<400> 48
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<213> Homo sapien

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<400> 66
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<210> 67
<211> 3444
<212> DNA
<213> Homo sapien

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<400> 67

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<210> 68

<211> 2081

<212> DNA

<213> Homo sapien

<400> 68

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<210> 69
 <211> 845
 <212> DNA
 <213> Homo sapien

<400> 69
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<210> 70
 <211> 853
 <212> DNA
 <213> Homo sapien

<400> 70
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<210> 71
 <211> 853
 <212> DNA
 <213> Homo sapien

<400> 71
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<211> 1666
<212> DNA
<213> Homo sapien

<400> 72
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<210> 73

<211> 1542

<212> DNA

<213> Homo sapien

<400> 73

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<210> 74
<211> 1958
<212> DNA
<213> Homo sapien

<400> 74
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<211> 2419

<212> DNA

<213> Homo sapien

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10/538002
JC17 Rec'd PCT/PTO 03 JUN 2005

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Ala Glu Gly Val Ala Ala Pro Ala Asp Pro Glu Met Val Thr Leu Pro
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Leu Gln Pro Ser Ser Thr Met Gly Gln Val Gly Arg Gln Leu Ala Ile
65 70 75 80

Ile Gly Asp Asp Ile Asn Arg Arg Tyr Asp Ser Glu Phe Gln Thr Met
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Leu Gln His Leu Gln Pro Thr Ala Glu Asn Ala Tyr Glu Tyr Phe Thr
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Lys Ile Ala Thr Ser Leu Phe Glu Ser Gly Ile Asn Trp Gly Arg Val
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His Gly Leu Thr Gly Phe Leu Gly Gln Val Thr Arg Phe Val Val Asp
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Phe Met Leu His His Cys Ile Ala Arg Trp Ile Ala Gln Arg Gly Gly
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 20 25 30

Pro Gly Asp Pro Leu Arg Gly Arg Leu His Ala Ala Ser Leu His Cys
 35 40 45

Pro Val Asp Cys Thr Glu Gly Trp Leu Gly Glu Tyr Pro Arg Thr Ala
 50 55 60

Met Ser Ser Leu Leu Leu Gly Leu Pro Leu Ser Gln Ala Pro Pro Leu
 65 70 75 80

Pro Arg Val Pro Ile Ser Ser Ala Ser Leu Ser Val Thr Thr Leu Phe
 85 90 95

Leu Pro Ala Gly Gly Ser Pro Glu Leu Gly Gln Trp Ser His Pro Glu
 100 105 110

Arg Ala Gly Gly Ser Gly Cys Gly Ser Val Gly Pro Val Cys Gly Thr
 115 120 125

Lys Ile Leu Gln Ile Met Thr Pro Lys Gly Ala Leu Trp Gly Pro Gly
 130 135 140

Ser Asp Pro Cys Leu Asp Leu Ser Glu Val Phe Ala Phe Ser Ala Pro
 145 150 155 160

Leu Gln Gly Ser Pro Leu Lys Ser Thr Glu Ala Leu Ala Ser Val His
 165 170 175

Ser Ser Phe Gly Gly Pro Leu Arg Gly Gly Gln Ser Gly Cys Arg Gly
 180 185 190

Thr Ser Thr Leu His Gly Ala Ser Gly Pro Ser Leu Trp Ala Gln Gly
 195 200 205

Leu Trp Pro Ser Pro Pro Ser Ala Leu Trp Asp Leu Leu Ser Pro Val
 210 215 220

Cys
 225

<210> 97
 <211> 284
 <212> PRT
 <213> Homo sapien

<400> 97

Met Ala Pro Leu His Ser Ser Leu Gly Asn Lys Arg Asn Ser Ile Ser
 1 5 10 15

Lys Lys Lys Lys Ile Tyr Ser Cys Phe Leu Asn Leu Ala Glu Arg Ile
 20 25 30

Arg Ile Pro Glu Pro Trp Ile Thr Pro Pro Asp Leu Gln Glu Lys Ile
 35 40 45

His Ile Phe Ala Gln Lys Cys Leu Phe Leu Thr Glu Ser Leu Lys Gln
 50 55 60

Phe Thr Glu Lys Met Gln Ser Asp Met Glu Lys Ile Gln Glu Leu Arg
 65 70 75 80

Glu Ala Gln Leu Tyr Ser Val Asp Val Thr Leu Asp Pro Asp Thr Ala
 85 90 95

Tyr Pro Ser Leu Ile Leu Ser Asp Asn Leu Arg Gln Val Arg Tyr Ser
 100 105 110

Tyr Leu Gln Gln Asp Leu Pro Asp Asn Pro Glu Arg Phe Asn Leu Phe
 115 120 125

Pro Cys Val Leu Gly Ser Pro Cys Phe Ile Ala Gly Arg His Tyr Trp
 130 135 140

Glu Val Glu Val Gly Asp Lys Ala Lys Trp Thr Ile Gly Val Cys Glu
 145 150 155 160

Asp Ser Val Cys Arg Lys Gly Gly Val Thr Ser Ala Pro Gln Asn Gly
 165 170 175

Phe Trp Ala Val Ser Leu Trp Tyr Gly Lys Glu Tyr Trp Ala Leu Thr
 180 185 190

Ser Pro Met Thr Ala Leu Pro Leu Arg Thr Pro Leu Gln Arg Val Gly
 195 200 205

Ile Phe Leu Asp Tyr Asp Ala Gly Glu Val Ser Phe Tyr Asn Val Thr

210 215 220
 Glu Arg Cys His Thr Phe Thr Phe Ser His Ala Thr Phe Cys Gly Pro
 225 230 235 240
 Val Arg Pro Tyr Phe Ser Leu Ser Tyr Ser Gly Gly Lys Ser Ala Ala
 245 250 255
 Pro Leu Ile Ile Cys Pro Met Ser Gly Ile Asp Gly Phe Ser Gly His
 260 265 270
 Val Gly Asn His Gly His Ser Met Glu Thr Ser Pro
 275 280
 <210> 98
 <211> 321
 <212> PRT
 <213> Homo sapien
 <400> 98
 Lys His Lys Ile Ser Trp Val Trp Trp Arg Met Pro Val Ile Pro Ala
 1 5 10 15
 Thr Gln Glu Ala Glu Ala Gly Glu Ser Leu Glu Pro Gly Arg Gln Arg
 20 25 30
 Leu Arg Trp Ala Glu Met Ala Pro Leu His Ser Ser Leu Gly Asn Lys
 35 40 45
 Arg Asn Ser Ile Ser Lys Lys Lys Lys Ile Tyr Ser Cys Phe Leu Asn
 50 55 60
 Leu Ala Glu Arg Ile Arg Ile Pro Glu Pro Trp Ile Thr Pro Pro Asp
 65 70 75 80
 Leu Gln Glu Lys Ile His Ile Phe Ala Gln Lys Cys Leu Phe Leu Thr
 85 90 95
 Glu Ser Leu Lys Gln Phe Thr Glu Lys Met Gln Ser Asp Met Glu Lys
 100 105 110
 Ile Gln Glu Leu Arg Glu Ala Gln Leu Tyr Ser Val Asp Val Thr Leu
 115 120 125
 Asp Pro Asp Thr Ala Tyr Pro Ser Leu Ile Leu Ser Asp Asn Leu Arg
 130 135 140

Gln Val Arg Tyr Ser Tyr Leu Gln Gln Asp Leu Pro Asp Asn Pro Glu
145 150 155 160

Arg Phe Asn Leu Phe Pro Cys Val Leu Gly Ser Pro Cys Phe Ile Ala
165 170 175

Gly Arg His Tyr Trp Glu Val Glu Val Gly Asp Lys Ala Lys Trp Thr
180 185 190

Ile Gly Val Cys Glu Asp Ser Val Cys Arg Lys Gly Gly Val Thr Ser
195 200 205

Ala Pro Gln Asn Gly Phe Trp Ala Val Ser Leu Trp Tyr Gly Lys Glu
210 215 220

Tyr Trp Ala Leu Thr Ser Pro Met Thr Ala Leu Pro Leu Arg Thr Pro
225 230 235 240

Leu Gln Arg Val Gly Ile Phe Leu Asp Tyr Asp Ala Gly Glu Val Ser
245 250 255

Phe Tyr Asn Val Thr Glu Arg Cys His Thr Phe Thr Phe Ser His Ala
260 265 270

Thr Phe Cys Gly Pro Val Arg Pro Tyr Phe Ser Leu Ser Tyr Ser Gly
275 280 285

Gly Lys Ser Ala Ala Pro Leu Ile Ile Cys Pro Met Ser Gly Ile Asp
290 295 300

Gly Phe Ser Gly His Val Gly Asn His Gly His Ser Met Glu Thr Ser
305 310 315 320

Pro

<210> 99
<211> 50
<212> PRT
<213> Homo sapien

<400> 99

Thr Ile Tyr Gly Pro Lys Val Ala Lys Ile Leu Arg Ala Ser Val Glu
1 5 10 15

Leu Leu Asp Glu Met Lys Phe Ser Leu Glu Lys Leu His Gln Gly Ile

20 25 30
 Thr Val Ser Asp Pro Pro Phe Asp Thr Gln Pro Arg Pro Asp Asp Ser
 35 40 45
 Phe Ser
 50
 <210> 100
 <211> 121
 <212> PRT
 <213> Homo sapien
 <400> 100
 Ser Ser Arg Trp Arg Ser Cys Thr Lys Ala Ser Gln Ser Gln Thr Leu
 1 5 10 15
 Pro Leu Thr Pro Ser Pro Gly Pro Met Thr Ala Phe Pro Glu Asp Pro
 20 25 30
 Gly His Ala Ala Val Pro Pro His Gly Gln Met Asp Thr Gln Ser Leu
 35 40 45
 Gly Gly His Cys Trp His Gly Val Ser Ala Arg His Leu Pro Pro Ala
 50 55 60
 Pro Pro Asp Gly Pro Thr Arg Gly Cys Ala Asp Val Gly Thr Thr Glu
 65 70 75 80
 Pro Arg Cys Thr Leu Asp Gln Gly Ala Gly Pro Ala Ser Gly Arg Pro
 85 90 95
 Pro Thr Asn Leu Phe Cys Pro Ala Glu Val Val Gly Gly Ala Ser Trp
 100 105 110
 Gly Ala Arg Phe Pro Gln Leu Trp Val
 115 120
 <210> 101
 <211> 386
 <212> PRT
 <213> Homo sapien
 <400> 101
 Met Phe Asp Thr Thr Pro His Ser Gly Arg Ser Thr Pro Ser Ser Ser
 1 5 10 15

Pro Ser Leu Arg Lys Arg Leu Gln Leu Leu Pro Pro Ser Arg Pro Pro
 20 25 30

Pro Glu Pro Glu Pro Gly Thr Met Val Glu Lys Gly Ser Asp Ser Ser
 35 40 45

Ser Glu Lys Gly Gly Val Pro Gly Thr Pro Ser Thr Gln Ser Leu Gly
 50 55 60

Ser Arg Asn Phe Ile Arg Asn Ser Lys Lys Met Gln Ser Trp Tyr Ser
 65 70 75 80

Met Leu Ser Pro Thr Tyr Lys Gln Arg Asn Glu Asp Phe Arg Lys Leu
 85 90 95

Phe Ser Lys Leu Pro Glu Ala Glu Arg Leu Ile Val Asp Tyr Ser Cys
 100 105 110

Ala Leu Gln Arg Glu Ile Leu Leu Gln Gly Arg Leu Tyr Leu Ser Glu
 115 120 125

Asn Trp Ile Cys Phe Tyr Ser Asn Ile Phe Arg Trp Glu Thr Thr Ile
 130 135 140

Ser Ile Gln Leu Lys Glu Val Thr Cys Leu Lys Lys Glu Lys Thr Ala
 145 150 155 160

Lys Leu Ile Pro Asn Ala Ile Gln Ile Cys Thr Glu Ser Glu Lys His
 165 170 175

Phe Phe Thr Ser Phe Gly Ala Arg Asp Arg Cys Phe Leu Leu Ile Phe
 180 185 190

Arg Leu Trp Gln Asn Ala Leu Leu Glu Lys Thr Leu Ser Pro Arg Glu
 195 200 205

Leu Trp His Leu Val His Gln Cys Tyr Gly Ser Glu Leu Gly Leu Thr
 210 215 220

Ser Glu Asp Glu Asp Tyr Val Ser Pro Leu Gln Leu Asn Gly Leu Gly
 225 230 235 240

Thr Pro Lys Glu Val Gly Asp Val Ile Ala Leu Ser Asp Ile Thr Ser
 245 250 255

Ser Gly Ala Ala Asp Arg Ser Gln Glu Pro Ser Pro Val Gly Ser Arg

260 265 270
 Arg Gly His Val Thr Pro Asn Leu Ser Arg Ala Ser Ser Asp Ala Asp
 275 280 285
 His Gly Ala Glu Glu Asp Lys Glu Glu Gln Val Asp Ser Gln Pro Asp
 290 295 300
 Ala Ser Ser Ser Gln Thr Val Thr Pro Val Ala Glu Pro Pro Ser Thr
 305 310 315 320
 Glu Pro Thr Gln Pro Asp Gly Pro Thr Thr Leu Gly Pro Leu Asp Leu
 325 330 335
 Leu Pro Ser Glu Glu Leu Leu Thr Asp Thr Ser Asn Ser Ser Ser Ser
 340 345 350
 Thr Gly Glu Glu Gly Glu Ala Gly Gly Pro Asn Ser Phe Ala Ser Gly
 355 360 365
 Thr Cys Lys Pro Arg Ser Val Leu Ser Lys Arg Gly Trp Ile Arg Pro
 370 375 380

Gln His
385

<210> 102
 <211> 190
 <212> PRT
 <213> Homo sapien

<400> 102

Met Phe Gly Phe Asn Lys Val Ser Leu Phe Pro Ser Leu Ser Leu Cys
1 5 10 15

Pro Ser Ala Phe Pro Ser Leu Ser Ser Pro Ser Leu Pro Gly Phe Ser
20 25 30

Leu Leu Leu Gly Leu Cys Gly Pro Ser Pro Pro Ser Leu Pro Gly Trp
35 40 45

Gly Arg Arg Arg Asp Ala Ala Gly Arg Gly Lys Glu Gly Gly Val Ala
50 55 60

Asp Ala Ala Ala Ala Ser Gly Gly Ser Gly Leu Leu Cys Gly Arg Leu
65 70 75 80

Gly Arg Val Gly Ala Ala Ala Glu Gly Gln Ala Gly Ala Leu Arg
85 90 95

Gly Arg Pro Ala Gln Pro Ser Pro Ala Gln Pro Ser Pro Ala Leu Pro
100 105 110

Cys Pro Ala Leu Pro Cys Ala Arg Gly Ala Pro Thr Ala Pro His Pro
115 120 125

Cys Ser Thr Pro His Pro Thr Leu Ala Gly Ala Arg Gln Ala Ala Pro
130 135 140

His Arg Ser Gly Asn Gly Cys Ser Ser Cys Pro Gln Ala Gly Pro His
145 150 155 160

Leu Ser Gln Asn Gln Ala Pro Trp Trp Arg Arg Asp Gln Ile Ala Pro
165 170 175

Gln Arg Arg Val Gly Cys Leu Gly Pro Pro Ala Pro Arg Ala
180 185 190

<210> 103

<211> 442

<212> PRT

<213> Homo sapien

<400> 103

Arg Arg Gly Gly Leu Arg Arg Leu Arg Pro Phe Val Arg Ala Val Gly
1 5 10 15

Ser Gly Gly Gly Gly Gly Arg Gly Arg Pro Gly Arg Cys Pro Ala Gly
20 25 30

Thr Pro Ser Ala Ala Gln Pro Arg Ala Ala Gln Pro Cys Pro Ala Leu
35 40 45

Pro Cys Pro Ala Leu Arg Pro Gly Arg Ala His Arg Ala Ala Ser Met
50 55 60

Phe Asp Thr Thr Pro His Ser Gly Arg Ser Thr Pro Ser Ser Ser Pro
65 70 75 80

Ser Leu Arg Lys Arg Leu Gln Leu Leu Pro Pro Ser Arg Pro Pro Pro
85 90 95

Glu Pro Glu Pro Gly Thr Met Val Glu Lys Gly Ser Asp Ser Ser Ser

100	105	110
Glu Lys Gly Gly Val Pro Gly Thr Pro Ser Thr Gln Ser Leu Gly Ser 115	120	125
Arg Asn Phe Ile Arg Asn Ser Lys Lys Met Gln Ser Trp Tyr Ser Met 130	135	140
Leu Ser Pro Thr Tyr Lys Gln Arg Asn Glu Asp Phe Arg Lys Leu Phe 145	150	155 160
Ser Lys Leu Pro Glu Ala Glu Arg Leu Ile Val Asp Tyr Ser Cys Ala 165	170	175
Leu Gln Arg Glu Ile Leu Leu Gln Gly Arg Leu Tyr Leu Ser Glu Asn 180	185	190
Trp Ile Cys Phe Tyr Ser Asn Ile Phe Arg Trp Glu Thr Thr Ile Ser 195	200	205
Ile Gln Leu Lys Glu Val Thr Cys Leu Lys Lys Glu Lys Thr Ala Lys 210	215	220
Leu Ile Pro Asn Ala Ile Gln Ile Cys Thr Glu Ser Glu Lys His Phe 225	230	235 240
Phe Thr Ser Phe Gly Ala Arg Asp Arg Cys Phe Leu Leu Ile Phe Arg 245	250	255
Leu Trp Gln Asn Ala Leu Leu Glu Lys Thr Leu Ser Pro Arg Glu Leu 260	265	270
Trp His Leu Val His Gln Cys Tyr Gly Ser Glu Leu Gly Leu Thr Ser 275	280	285
Glu Asp Glu Asp Tyr Val Ser Pro Leu Gln Leu Asn Gly Leu Gly Thr 290	295	300
Pro Lys Glu Val Gly Asp Val Ile Ala Leu Ser Asp Ile Thr Ser Ser 305	310	315 320
Gly Ala Ala Asp Arg Ser Gln Glu Pro Ser Pro Val Gly Ser Arg Arg 325	330	335
Gly His Val Thr Pro Asn Leu Ser Arg Ala Ser Ser Asp Ala Asp His 340	345	350

Gly Ala Glu Glu Asp Lys Glu Glu Gln Val Asp Ser Gln Pro Asp Ala
 355 360 365

Ser Ser Ser Gln Thr Val Thr Pro Val Ala Glu Pro Pro Ser Thr Glu
 370 375 380

Pro Thr Gln Pro Asp Gly Pro Thr Thr Leu Gly Pro Leu Asp Leu Leu
 385 390 395 400

Pro Ser Glu Glu Leu Leu Thr Asp Thr Ser Asn Ser Ser Ser Ser Thr
 405 410 415

Gly Glu Glu Gly Leu Gly Cys Pro Ala Ser Arg Pro Leu Arg Pro Pro
 420 425 430

Pro His Gln Leu Cys Leu Pro Cys Gly Arg
 435 440

<210> 104
 <211> 99
 <212> PRT
 <213> Homo sapien

<400> 104

Met Glu Asp Pro Ser Val Arg Cys Ser Phe Gln Leu Thr Ser Gly Arg
 1 5 10 15

Arg Thr Ser Ala Met Lys Val Thr Gly Ile Phe Leu Leu Ser Ala Leu
 20 25 30

Ala Leu Leu Ser Leu Ser Gly Asn Thr Gly Ala Asp Ser Leu Gly Arg
 35 40 45

Glu Ala Lys Cys Tyr Asn Glu Leu Asn Gly Cys Thr Lys Ile Tyr Asp
 50 55 60

Pro Val Cys Gly Thr Asp Gly Asn Thr Tyr Pro Asn Glu Cys Val Leu
 65 70 75 80

Cys Phe Glu Asn Arg Lys Arg Gln Thr Ser Ile Leu Ile Gln Lys Ser
 85 90 95

Gly Pro Cys

151/383

<210> 105
 <211> 106
 <212> PRT
 <213> Homo sapien

<400> 105

Ala Leu Asp Val Lys Val Ser His Glu Gly Gly Arg Ser Val Leu Pro
 1 5 10 15

Gln Ser Lys Tyr Ser Val Arg His His Ile Pro Tyr Pro Ser Asn Gly
 20 25 30

Glu Leu His Ser Gln Tyr His Gly Tyr Tyr Val Lys Leu Asn Ala Pro
 35 40 45

Gln His Pro Pro Val Asp Val Glu Asp Gly Asp Gly Ser Ser Gln Ser
 50 55 60

Ser Ser Ala Leu Val His Lys Pro Ser Ala Asn Lys Trp Ser Pro Ser
 65 70 75 80

Lys Ser Val Thr Lys Pro Val Ala Lys Glu Ser Lys Ala Glu Pro Lys
 85 90 95

Ala Lys Lys Ser Glu Leu Ala Ile Pro Lys
 100 105

<210> 106
 <211> 93
 <212> PRT
 <213> Homo sapien

<220>
 <221> MISC_FEATURE
 <222> (93)..(93)
 <223> X=any amino acid

<400> 106

Ala Leu Asp Val Lys Val Ser His Glu Gly Gly Arg Ser Val Leu Pro
 1 5 10 15

Gln Ser Lys Tyr Ser Val Arg His His Ile Pro Tyr Pro Ser Asn Gly
 20 25 30

Glu Leu His Ser Gln Tyr His Gly Tyr Tyr Val Lys Leu Asn Ala Pro
 35 40 45

Gln His Pro Pro Val Asp Val Glu Asp Gly Asp Gly Ser Ser Gln Ser

152/383

50

55

60

Ser Ser Ala Leu Val His Lys Pro Ser Ala Asn Lys Trp Ser Pro Ser
65 70 75 80

Lys Ser Val Thr Lys Pro Val Ala Lys Glu Ser Lys Xaa
85 90

<210> 107
<211> 100
<212> PRT
<213> Homo sapien

<400> 107

Met Tyr Met Tyr Ile Gln Thr Thr Thr Leu Thr Val Ser Met Ser Leu
1 5 10 15

Ser Ala Ser Val Ser Leu Gly Met Leu Tyr Met Pro Lys Val Tyr Ile
20 25 30

Ile Ile Phe His Pro Glu Gln Asn Val Gln Lys Arg Lys Arg Ser Phe
35 40 45

Lys Ala Val Val Thr Ala Ala Thr Met Gln Ser Lys Leu Ile Gln Lys
50 55 60

Gly Asn Asp Arg Pro Asn Gly Glu Val Lys Ser Glu Leu Cys Glu Ser
65 70 75 80

Leu Glu Thr Asn Thr Ser Ser Thr Lys Thr Thr Tyr Ile Ser Tyr Ser
85 90 95

Asn His Ser Ile
100

<210> 108
<211> 558
<212> PRT
<213> Homo sapien

<400> 108

Trp Lys Phe Thr Val Thr Phe Lys Ser Arg Lys Leu Ala Asn Ala His
1 5 10 15

Arg Ala Phe Ser Pro Trp Ala Leu Met Val Ala Ser Arg Arg Cys Ser
20 25 30

Leu Arg Trp Cys Pro Phe Cys Cys Val Ala Arg Ile Asn Phe Gly Ser
35 40 45

Trp Ile Ala Ile Pro Pro Val Glu Lys Met Val Cys Glu Gly Lys Arg
50 55 60

Ser Ala Ser Cys Pro Cys Phe Phe Leu Leu Thr Ala Lys Phe Tyr Trp
65 70 75 80

Ile Leu Thr Met Met Gln Arg Thr His Ser Gln Glu Tyr Ala His Ser
85 90 95

Ile Arg Val Asp Gly Asp Ile Ile Leu Gly Gly Leu Phe Pro Val His
100 105 110

Ala Lys Gly Glu Arg Gly Val Pro Cys Gly Glu Leu Lys Lys Glu Lys
115 120 125

Gly Ile His Arg Leu Glu Ala Met Leu Tyr Ala Ile Asp Gln Ile Asn
130 135 140

Lys Asp Pro Asp Leu Leu Ser Asn Ile Thr Leu Gly Val Arg Ile Leu
145 150 155 160

Asp Thr Cys Ser Arg Asp Thr Tyr Ala Leu Glu Gln Ser Leu Thr Phe
165 170 175

Val Gln Ala Leu Ile Glu Lys Asp Ala Ser Asp Val Lys Cys Ala Asn
180 185 190

Gly Asp Pro Pro Ile Phe Thr Lys Pro Asp Lys Ile Ser Gly Val Ile
195 200 205

Gly Ala Ala Ala Ser Ser Val Ser Ile Met Val Ala Asn Ile Leu Arg
210 215 220

Leu Phe Lys Ile Pro Gln Ile Ser Tyr Ala Ser Thr Ala Pro Glu Leu
225 230 235 240

Ser Asp Asn Thr Arg Tyr Asp Phe Phe Ser Arg Val Val Pro Pro Asp
245 250 255

Ser Tyr Gln Ala Gln Ala Met Val Asp Ile Val Thr Ala Leu Gly Trp
260 265 270

Asn Tyr Val Ser Thr Leu Ala Ser Glu Gly Asn Tyr Gly Glu Ser Gly

275	280	285
Val Glu Ala Phe Thr Gln Ile Ser Arg Glu Ile Gly Gly Val Cys Ile		
290	295	300
Ala Gln Ser Gln Lys Ile Pro Arg Glu Pro Arg Pro Gly Glu Phe Glu		
305	310	315
Lys Ile Ile Lys Arg Leu Leu Glu Thr Pro Asn Ala Arg Ala Val Ile		
325	330	335
Met Phe Ala Asn Glu Asp Asp Ile Arg Arg Ile Leu Glu Ala Ala Lys		
340	345	350
Lys Leu Asn Gln Ser Gly His Phe Leu Trp Ile Gly Ser Asp Ser Trp		
355	360	365
Gly Ser Lys Ile Ala Pro Val Tyr Gln Gln Glu Glu Ile Ala Glu Gly		
370	375	380
Ala Val Thr Ile Leu Pro Lys Arg Ala Ser Ile Asp Gly Phe Asp Arg		
385	390	395
Tyr Phe Arg Ser Arg Thr Leu Ala Asn Asn Arg Arg Asn Val Trp Phe		
405	410	415
Ala Glu Phe Trp Glu Glu Asn Phe Gly Cys Lys Leu Gly Ser His Gly		
420	425	430
Lys Arg Asn Ser His Ile Lys Lys Cys Thr Gly Leu Glu Arg Ile Ala		
435	440	445
Arg Asp Ser Ser Tyr Glu Gln Glu Gly Lys Val Gln Phe Val Ile Asp		
450	455	460
Ala Val Tyr Ser Met Ala Tyr Ala Leu His Asn Met His Lys Asp Leu		
465	470	475
Cys Pro Gly Tyr Ile Gly Leu Cys Pro Arg Met Ser Thr Ile Asp Gly		
485	490	495
Lys Glu Leu Leu Gly Tyr Ile Arg Ala Val Asn Phe Asn Gly Cys Arg		
500	505	510
Arg Gly Ile Gln Met Ser Leu Pro Trp Pro Thr Leu Phe Thr Pro Ser		
515	520	525

Phe Ser Ser Ser Trp Ala Val Leu Ala Leu Leu Ser Leu Leu Met Lys
 530 535 540

Thr Glu Met Leu Leu Asp Val Met Ile Ser Ser Ser Ile Lys
 545 550 555

<210> 109
 <211> 501
 <212> PRT
 <213> Homo sapien

<400> 109

Met Val Cys Glu Gly Lys Arg Ser Ala Ser Cys Pro Cys Phe Phe Leu
 1 5 10 15

Leu Thr Ala Lys Phe Tyr Trp Ile Leu Thr Met Met Gln Arg Thr His
 20 25 30

Ser Gln Glu Tyr Ala His Ser Ile Arg Val Asp Gly Asp Ile Ile Leu
 35 40 45

Gly Gly Leu Phe Pro Val His Ala Lys Gly Glu Arg Gly Val Pro Cys
 50 55 60

Gly Glu Leu Lys Lys Glu Lys Gly Ile His Arg Leu Glu Ala Met Leu
 65 70 75 80

Tyr Ala Ile Asp Gln Ile Asn Lys Asp Pro Asp Leu Leu Ser Asn Ile
 85 90 95

Thr Leu Gly Val Arg Ile Leu Asp Thr Cys Ser Arg Asp Thr Tyr Ala
 100 105 110

Leu Glu Gln Ser Leu Thr Phe Val Gln Ala Leu Ile Glu Lys Asp Ala
 115 120 125

Ser Asp Val Lys Cys Ala Asn Gly Asp Pro Pro Ile Phe Thr Lys Pro
 130 135 140

Asp Lys Ile Ser Gly Val Ile Gly Ala Ala Ala Ser Ser Val Ser Ile
 145 150 155 160

Met Val Ala Asn Ile Leu Arg Leu Phe Lys Ile Pro Gln Ile Ser Tyr
 165 170 175

156/383

Ala Ser Thr Ala Pro Glu Leu Ser Asp Asn Thr Arg Tyr Asp Phe Phe
180 185 190

Ser Arg Val Val Pro Pro Asp Ser Tyr Gln Ala Gln Ala Met Val Asp
195 200 205

Ile Val Thr Ala Leu Gly Trp Asn Tyr Val Ser Thr Leu Ala Ser Glu
210 215 220

Gly Asn Tyr Gly Glu Ser Gly Val Glu Ala Phe Thr Gln Ile Ser Arg
225 230 235 240

Glu Ile Gly Gly Val Cys Ile Ala Gln Ser Gln Lys Ile Pro Arg Glu
245 250 255

Pro Arg Pro Gly Glu Phe Glu Lys Ile Ile Lys Arg Leu Leu Glu Thr
260 265 270

Pro Asn Ala Arg Ala Val Ile Met Phe Ala Asn Glu Asp Asp Ile Arg
275 280 285

Arg Ile Leu Glu Ala Ala Lys Lys Leu Asn Gln Ser Gly His Phe Leu
290 295 300

Trp Ile Gly Ser Asp Ser Trp Gly Ser Lys Ile Ala Pro Val Tyr Gln
305 310 315 320

Gln Glu Glu Ile Ala Glu Gly Ala Val Thr Ile Leu Pro Lys Arg Ala
325 330 335

Ser Ile Asp Gly Phe Asp Arg Tyr Phe Arg Ser Arg Thr Leu Ala Asn
340 345 350

Asn Arg Arg Asn Val Trp Phe Ala Glu Phe Trp Glu Glu Asn Phe Gly
355 360 365

Cys Lys Leu Gly Ser His Gly Lys Arg Asn Ser His Ile Lys Lys Cys
370 375 380

Thr Gly Leu Glu Arg Ile Ala Arg Asp Ser Ser Tyr Glu Gln Glu Gly
385 390 395 400

Lys Val Gln Phe Val Ile Asp Ala Val Tyr Ser Met Ala Tyr Ala Leu
405 410 415

His Asn Met His Lys Asp Leu Cys Pro Gly Tyr Ile Gly Leu Cys Pro

157/383

420

425

430

Arg Met Ser Thr Ile Asp Gly Lys Glu Leu Leu Gly Tyr Ile Arg Ala
 435 440 445

Val Asn Phe Asn Gly Cys Arg Arg Gly Ile Gln Met Ser Leu Pro Trp
 450 455 460

Pro Thr Leu Phe Thr Pro Ser Phe Ser Ser Ser Trp Ala Val Leu Ala
 465 470 475 480

Leu Leu Ser Leu Leu Met Lys Thr Glu Met Leu Leu Asp Val Met Ile
 485 490 495

Ser Ser Ser Ile Lys
 500

<210> 110
 <211> 338
 <212> PRT
 <213> Homo sapien

<400> 110

Trp Lys Phe Thr Val Thr Phe Lys Ser Arg Lys Leu Ala Asn Ala His
 1 5 10 15

Arg Ala Phe Ser Pro Trp Ala Leu Met Val Ala Ser Arg Arg Cys Ser
 20 25 30

Leu Arg Trp Cys Pro Phe Cys Cys Val Ala Arg Ile Asn Phe Gly Ser
 35 40 45

Trp Ile Ala Ile Pro Pro Val Glu Lys Met Val Cys Glu Gly Lys Arg
 50 55 60

Ser Ala Ser Cys Pro Cys Phe Phe Leu Leu Thr Ala Lys Phe Tyr Trp
 65 70 75 80

Ile Leu Thr Met Met Gln Arg Thr His Ser Gln Glu Tyr Ala His Ser
 85 90 95

Ile Arg Val Asp Gly Asp Ile Ile Leu Gly Gly Leu Phe Pro Val His
 100 105 110

Ala Lys Gly Glu Arg Gly Val Pro Cys Gly Glu Leu Lys Lys Glu Lys
 115 120 125

Gly Ile His Arg Leu Glu Ala Met Leu Tyr Ala Ile Asp Gln Ile Asn
 130 135 140

Lys Asp Pro Asp Leu Leu Ser Asn Ile Thr Leu Gly Val Arg Ile Leu
 145 150 155 160

Asp Thr Cys Ser Arg Asp Thr Tyr Ala Leu Glu Gln Ser Leu Thr Phe
 165 170 175

Val Gln Ala Leu Ile Glu Lys Asp Ala Ser Asp Val Lys Cys Ala Asn
 180 185 190

Gly Asp Pro Pro Ile Phe Thr Lys Pro Asp Lys Ile Ser Gly Val Ile
 195 200 205

Gly Ala Ala Ala Ser Ser Val Ser Ile Met Val Ala Asn Ile Leu Arg
 210 215 220

Leu Phe Lys Ile Pro Gln Ile Ser Tyr Ala Ser Thr Ala Pro Glu Leu
 225 230 235 240

Ser Asp Asn Thr Arg Tyr Asp Phe Phe Ser Arg Val Val Pro Pro Asp
 245 250 255

Ser Tyr Gln Ala Gln Ala Met Val Asp Ile Val Thr Ala Leu Gly Trp
 260 265 270

Asn Tyr Val Ser Thr Leu Ala Ser Glu Gly Asn Tyr Gly Glu Ser Gly
 275 280 285

Val Glu Ala Phe Thr Gln Ile Ser Arg Glu Ile Gly Tyr Pro Ser Leu
 290 295 300

Phe Gly Ile Gln Gly Cys Leu His Glu Cys Phe Ala Ile Leu Cys Gln
 305 310 315 320

Val Val Tyr Gln Phe Leu Leu Leu Met Gln Leu Ser Asp Ala Gln Thr
 325 330 335

Val Tyr

<210> 111
 <211> 281
 <212> PRT
 <213> Homo sapien

<400> 111

Met Val Cys Glu Gly Lys Arg Ser Ala Ser Cys Pro Cys Phe Phe Leu
 1 5 10 15

Leu Thr Ala Lys Phe Tyr Trp Ile Leu Thr Met Met Gln Arg Thr His
 20 25 30

Ser Gln Glu Tyr Ala His Ser Ile Arg Val Asp Gly Asp Ile Ile Leu
 35 40 45

Gly Gly Leu Phe Pro Val His Ala Lys Gly Glu Arg Gly Val Pro Cys
 50 55 60

Gly Glu Leu Lys Lys Glu Lys Gly Ile His Arg Leu Glu Ala Met Leu
 65 70 75 80

Tyr Ala Ile Asp Gln Ile Asn Lys Asp Pro Asp Leu Leu Ser Asn Ile
 85 90 95

Thr Leu Gly Val Arg Ile Leu Asp Thr Cys Ser Arg Asp Thr Tyr Ala
 100 105 110

Leu Glu Gln Ser Leu Thr Phe Val Gln Ala Leu Ile Glu Lys Asp Ala
 115 120 125

Ser Asp Val Lys Cys Ala Asn Gly Asp Pro Pro Ile Phe Thr Lys Pro
 130 135 140

Asp Lys Ile Ser Gly Val Ile Gly Ala Ala Ala Ser Ser Val Ser Ile
 145 150 155 160

Met Val Ala Asn Ile Leu Arg Leu Phe Lys Ile Pro Gln Ile Ser Tyr
 165 170 175

Ala Ser Thr Ala Pro Glu Leu Ser Asp Asn Thr Arg Tyr Asp Phe Phe
 180 185 190

Ser Arg Val Val Pro Pro Asp Ser Tyr Gln Ala Gln Ala Met Val Asp
 195 200 205

Ile Val Thr Ala Leu Gly Trp Asn Tyr Val Ser Thr Leu Ala Ser Glu
 210 215 220

Gly Asn Tyr Gly Glu Ser Gly Val Glu Ala Phe Thr Gln Ile Ser Arg
 225 230 235 240

Glu Ile Gly Tyr Pro Ser Leu Phe Gly Ile Gln Gly Cys Leu His Glu
 245 250 255

Cys Phe Ala Ile Leu Cys Gln Val Val Tyr Gln Phe Leu Leu Leu Met
 260 265 270

Gln Leu Ser Asp Ala Gln Thr Val Tyr
 275 280

<210> 112
 <211> 433
 <212> PRT
 <213> Homo sapien

<400> 112

Met Val Val Phe Leu Ser Gly Asp Asn Leu Ser Ser Pro Ser His Ser
 1 5 10 15

Gly Ile Ile Trp Gln Cys Leu Glu Thr Phe Trp Val Leu Thr Asn Arg
 20 25 30

Arg Arg Met Pro Leu Ala Ser Ser Arg Ser Ala Met Leu Leu Ser Ile
 35 40 45

Leu Gln Cys Pro Gly Gln Pro His Lys Asp Ser Ser Ser Leu Asn Val
 50 55 60

Asn Ser Ala Glu Val Glu Glu Pro Tyr Phe Thr Gly Thr Arg Gln Glu
 65 70 75 80

Glu Ser Val Cys Pro Arg Thr Leu Val Ile Ile Thr Cys Pro Leu Gln
 85 90 95

Tyr Ser Thr Thr Gln Arg Gln Cys Phe Leu Gly Asn Gly Phe Phe Ser
 100 105 110

Leu Gln Val Leu His Phe Glu Asn Val Lys Asp Val Pro Phe Gly Phe
 115 120 125

Gln Thr Val Thr Ser Asp Val Asn Lys Leu Ser Ser Phe Tyr Ser Leu
 130 135 140

Lys Leu Ile Lys Arg Leu Tyr Val Asp Lys Ser Leu Asn Leu Ser Thr
 145 150 155 160

161/383

Glu Phe Ile Ser Ser Thr Lys Arg Pro Tyr Ala Lys Glu Leu Glu Thr
165 170 175

Val Asp Phe Lys Asp Lys Leu Glu Glu Thr Lys Gly Gln Ile Asn Asn
180 185 190

Ser Ile Lys Asp Leu Thr Asp Gly His Phe Glu Asn Ile Leu Ala Asp
195 200 205

Asn Ser Val Asn Asp Gln Thr Lys Ile Leu Val Val Asn Ala Ala Tyr
210 215 220

Phe Val Gly Lys Trp Met Lys Lys Phe Pro Glu Ser Glu Thr Lys Glu
225 230 235 240

Cys Pro Phe Arg Val Asn Lys Thr Asp Thr Lys Pro Val Gln Met Met
245 250 255

Asn Met Glu Ala Thr Phe Cys Met Gly Asn Ile Asp Ser Ile Asn Cys
260 265 270

Lys Ile Ile Glu Leu Pro Phe Gln Asn Lys His Leu Ser Met Phe Ile
275 280 285

Leu Leu Pro Lys Asp Val Glu Asp Glu Ser Thr Gly Leu Glu Lys Ile
290 295 300

Glu Lys Gln Leu Asn Ser Glu Ser Leu Ser Gln Trp Thr Asn Pro Ser
305 310 315 320

Thr Met Ala Asn Ala Lys Val Lys Leu Ser Ile Pro Lys Phe Lys Val
325 330 335

Glu Lys Met Ile Asp Pro Lys Ala Cys Leu Glu Asn Leu Gly Leu Lys
340 345 350

His Ile Phe Ser Glu Asp Thr Ser Asp Phe Ser Gly Met Ser Glu Thr
355 360 365

Lys Gly Val Ala Leu Ser Asn Val Ile His Lys Val Cys Leu Glu Ile
370 375 380

Thr Glu Asp Gly Gly Asp Ser Ile Glu Val Pro Gly Ala Arg Ile Leu
385 390 395 400

Gln His Lys Asp Glu Leu Asn Ala Asp His Pro Phe Ile Tyr Ile Ile

162/383

405

410

415

Arg His Asn Lys Thr Arg Asn Ile Ile Phe Phe Gly Lys Phe Cys Ser
 420 425 430

Pro

<210> 113
 <211> 705
 <212> PRT
 <213> Homo sapien

<400> 113

Met Glu Arg Met Trp Thr Ser Glu Glu Phe Ser Phe Lys Lys Asn Ile
 1 5 10 15

Met Lys Tyr Ile Leu Ile Thr Gln Gly Leu Leu Leu Val Glu Val Tyr
 20 25 30

Asn Leu Asp Thr Ser Thr Phe Cys Phe Cys Cys Ser Thr Val His Lys
 35 40 45

Thr Phe Ser Asn Leu Gln Gly Lys Ile Val Glu Val Val Glu Val Lys
 50 55 60

Leu Lys Phe Lys Ile Asp Ser Val Asn Thr Ile Gly Lys Glu Ala Glu
 65 70 75 80

Leu Arg Ile Phe Trp Leu Phe Met Cys Ser Val Leu Leu Ser Ser His
 85 90 95

Arg Ser Cys Val Val Thr Gln Asp Ser Gly Ser Thr Lys Pro Glu Leu
 100 105 110

Thr Gly Trp Ile Asp Leu Gln Pro Ile Phe Phe His Tyr Thr Ala Ala
 115 120 125

Phe Leu Phe Leu Lys Lys Gln Lys Ser Met Glu Gln Leu Leu Gln Lys
 130 135 140

Glu Ala Pro Leu Phe Asn Trp Leu Thr Glu Ser Met Asn His Cys Arg
 145 150 155 160

Phe Ala Cys Pro Pro Val Cys Phe Ser His Arg Phe Tyr Leu Ser Glu
 165 170 175

Trp Leu Leu His Leu Asn Thr Val Ala Met Val Ser Glu Gln Leu Lys
 180 185 190

Thr Ser Phe Leu His Leu His Ser Lys Gly Phe Ile Phe Ser Arg Asn
 195 200 205

Lys Val Val Leu Gly Cys Phe Asn Ser Val Asp His Leu Glu Thr Arg
 210 215 220

Glu Gln Gly Pro Trp Ile Thr Met Ser Thr Leu Gln Val Phe Gly Asn
 225 230 235 240

Ala Gly Lys Gly Leu His Ser Ser Asn Leu Leu Thr Ser Phe Leu Ser
 245 250 255

Val Arg Pro Met Leu Ala Cys Asn Tyr Ile Phe Leu Asn Leu Lys Thr
 260 265 270

Lys Glu Ile Ser Asp Ile Phe Ser Val Ser Phe Phe Ser Phe His Ser
 275 280 285

Ser Leu Lys Ser His Tyr Cys Ile Thr Phe Gln Ile Met Thr Trp Ile
 290 295 300

Glu Gly Ser Leu Phe Cys Gln Gly Leu Cys Glu Val Asn Ile Arg Ile
 305 310 315 320

Ser Thr Thr Thr Lys Leu Lys Asn Glu Ala Ala Leu Thr Glu Met Leu
 325 330 335

Ala Lys Thr Asn Ser Leu Asp Cys Phe Cys His His Leu Leu Thr Trp
 340 345 350

Asn Ser Phe His Ile Tyr Phe Ser Tyr Glu Glu Ile Gln Cys Gln Ser
 355 360 365

Asp His Val Thr Ser Lys Gln Asn Phe Ile Glu Ala Tyr Pro Cys Leu
 370 375 380

Asn Tyr Ser Lys Ile Lys Tyr Asn Lys Val Asn Tyr Phe Ala Leu Cys
 385 390 395 400

Ser Ser Ile Val Leu Ser Tyr Ile Tyr Ile Leu Ile Cys Ile Leu Leu
 405 410 415

Ser Lys Val Ser Glu Thr Thr Cys Trp Arg Ala Val Ala Phe Arg Gln
 420 425 430

His Gln His His Leu Lys Ala Leu Leu Asn Thr His Tyr Trp Lys Arg
 435 440 445

Gly Glu Asn Thr Gly Ile Met Pro Val Ile Pro Val Leu Trp Glu Thr
 450 455 460

Glu Ala Gly Gly Ser Arg Gly Ala Gln Glu Phe Lys Ile Arg Leu Gly
 465 470 475 480

Asn Thr Ala Arg Pro Leu Ser Leu Gln Lys Gln Lys Gln Lys Thr Asn
 485 490 495

Arg His Gly Ser Ala Tyr Leu Trp Ser Glu Leu Leu Gly Ser Leu Arg
 500 505 510

Gln Glu Asp His Leu Asn Pro Gly Val Arg Gly Cys Ser Glu Leu Leu
 515 520 525

Leu Gly Gln Leu Gln Ser Ser Leu Gly Ser Lys Val Arg Pro Cys Leu
 530 535 540

Leu Lys Lys Gln Asn Gln Lys Leu Asp Cys Trp Gly Pro Pro Arg Val
 545 550 555 560

Ser Asp Ser Val Gly Leu Ala Val Gly Met Val Gly Leu Val Ile Cys
 565 570 575

Leu Ser Asn Lys Arg Pro Gly Asn Ala Pro Ala Ala Gly Pro Gly Pro
 580 585 590

His Phe Ala Asp Tyr Tyr Ser Glu Lys Ser Thr Asn Ser Asp Val Gly
 595 600 605

Phe Leu Leu Phe Leu Ile Ser Glu Phe Ile Trp Gly Arg Leu Phe Asn
 610 615 620

Leu Val Asp Pro His Leu Leu Ser Cys Glu Val Glu Val Asn Ala Thr
 625 630 635 640

Cys Leu Glu Thr Val Arg Met Arg Asn Ser Glu Leu Lys Tyr Gln Ala
 645 650 655

Gln Arg Ala Trp Met Leu Glu Glu Met Leu Thr Pro Met Val Arg Pro

165/383

660

665

670

Ser Leu Thr Leu Leu Ser Tyr Lys Val Arg Ser Glu Ile Gln Tyr Leu
 675 680 685

Leu Arg Phe Leu Ser Gly Val Lys Cys Cys Asp Ser Lys Ser Leu Ile
 690 695 700

Leu
 705

<210> 114
 <211> 226
 <212> PRT
 <213> Homo sapien

<400> 114

Leu Ile Ile Asn Asp Cys Tyr Ser His Ser Ile Gly Gly Val Val Leu
 1 5 10 15

Val Asn Leu Ala Gly Ser Glu Lys Pro Ala Gly Arg Asp Thr Val Gly
 20 25 30

Ser Ile Trp Ser Leu Ala Gly Ala Met Leu Tyr Ala Val Tyr Ile Val
 35 40 45

Met Ile Lys Arg Lys Val Asp Arg Glu Asp Lys Leu Asp Ile Pro Met
 50 55 60

Phe Phe Gly Phe Val Gly Leu Phe Asn Leu Leu Leu Trp Pro Gly
 65 70 75 80

Phe Phe Leu Leu His Tyr Thr Gly Phe Glu Asp Phe Glu Phe Pro Asn
 85 90 95

Lys Val Val Leu Met Cys Ile Ile Ile Asn Gly Leu Ile Gly Thr Val
 100 105 110

Leu Ser Glu Phe Leu Trp Leu Trp Gly Cys Phe Leu Thr Ser Ser Leu
 115 120 125

Ile Gly Thr Leu Ala Leu Ser Leu Thr Ile Pro Leu Ser Ile Ile Ala
 130 135 140

Asp Met Cys Met Gln Lys Val Gln Phe Ser Trp Leu Phe Phe Ala Gly
 145 150 155 160

Ala Ile Pro Val Phe Phe Ser Phe Phe Ile Val Thr Leu Leu Cys His
 165 170 175

Tyr Asn Asn Trp Asp Pro Val Met Val Gly Ile Arg Arg Ile Phe Ala
 180 185 190

Phe Ile Cys Arg Lys His Arg Ile Gln Arg Val Pro Glu Asp Ser Glu
 195 200 205

Gln Cys Glu Ser Leu Ile Ser Met His Ser Val Ser Gln Glu Asp Gly
 210 215 220

Ala Ser
 225

<210> 115
 <211> 570
 <212> PRT
 <213> Homo sapien

<400> 115

Met Val Pro Pro Arg Arg His Arg Gly Ala Gly Arg Pro Gly Val Leu
 1 5 10 15

Ser Ser Ser Pro Pro Phe Arg Leu Arg Ser Ala Lys Phe Ser Gly Ile
 20 25 30

Ala Leu Glu Asp Leu Arg Arg Ala Leu Lys Thr Arg Leu Gln Met Val
 35 40 45

Cys Val Phe Val Met Asn Arg Met Asn Ser Gln Asn Ser Gly Phe Thr
 50 55 60

Gln Arg Arg Arg Met Ala Leu Gly Ile Val Ile Leu Leu Leu Val Asp
 65 70 75 80

Val Ile Trp Val Ala Ser Ser Glu Leu Thr Ser Tyr Val Phe Thr Gln
 85 90 95

Tyr Asn Lys Pro Phe Phe Ser Thr Phe Ala Lys Thr Ser Met Phe Val
 100 105 110

Leu Tyr Leu Leu Gly Phe Ile Ile Trp Lys Pro Trp Arg Gln Gln Cys
 115 120 125

Thr Arg Gly Leu Arg Gly Lys His Ala Ala Phe Phe Ala Asp Ala Glu

130	135	140
Gly Tyr Phe Ala Ala Cys Thr Thr Asp Thr Thr Met Asn Ser Ser Leu 145	150	155 160
Ser Glu Pro Leu Tyr Val Pro Val Lys Phe His Asp Leu Pro Ser Glu 165	170	175
Lys Pro Glu Ser Thr Asn Ile Asp Thr Glu Lys Thr Pro Lys Lys Ser 180	185	190
Arg Val Arg Phe Ser Asn Ile Met Glu Ile Arg Gln Leu Pro Ser Ser 195	200	205
His Ala Leu Glu Ala Lys Leu Ser Arg Met Ser Tyr Pro Val Lys Glu 210	215	220
Gln Glu Ser Ile Leu Lys Thr Val Gly Lys Leu Thr Ala Thr Gln Val 225	230	235 240
Ala Lys Ile Ser Phe Phe Phe Cys Phe Val Trp Phe Leu Ala Asn Leu 245	250	255
Ser Tyr Gln Glu Ala Leu Ser Asp Thr Gln Val Ala Ile Val Asn Ile 260	265	270
Leu Ser Ser Thr Ser Gly Leu Phe Thr Leu Ile Leu Ala Ala Val Phe 275	280	285
Pro Ser Asn Ser Gly Asp Arg Phe Thr Leu Ser Lys Leu Leu Ala Val 290	295	300
Ile Leu Ser Ile Gly Gly Val Val Leu Val Asn Leu Ala Gly Ser Glu 305	310	315 320
Lys Pro Ala Gly Arg Asp Thr Val Gly Ser Ile Trp Ser Leu Ala Gly 325	330	335
Ala Met Leu Tyr Ala Val Tyr Ile Val Met Ile Lys Arg Lys Val Asp 340	345	350
Arg Glu Asp Lys Leu Asp Ile Pro Met Phe Phe Gly Phe Val Gly Leu 355	360	365
Phe Asn Leu Leu Leu Leu Trp Pro Gly Phe Phe Leu Leu His Tyr Thr 370	375	380

Gly Phe Glu Asp Phe Glu Phe Pro Asn Lys Val Val Leu Met Cys Ile
385 390 395 400

Ile Ile Asn Gly Leu Ile Gly Thr Val Leu Ser Glu Phe Leu Trp Leu
405 410 415

Trp Gly Cys Phe Leu Thr Ser Ser Leu Ile Gly Thr Leu Ala Leu Ser
420 425 430

Leu Thr Ile Pro Leu Ser Ile Ile Ala Asp Met Cys Met Gln Lys Val
435 440 445

Gln Phe Ser Trp Leu Phe Phe Ala Gly Ala Ile Pro Val Phe Phe Ser
450 455 460

Phe Phe Ile Val Thr Leu Leu Cys His Tyr Asn Asn Trp Asp Pro Val
465 470 475 480

Met Val Gly Ile Arg Arg Ile Phe Ala Phe Ile Cys Arg Lys His Arg
485 490 495

Ile Gln Arg Trp Asn Leu Ala Leu Ser Pro Lys Leu Glu Cys Ser Gly
500 505 510

Glu Ile Ser Gly His Cys Asn Leu Tyr Leu Leu Gly Ser Ser Asp Ser
515 520 525

Pro Ala Ser Ala Ser Arg Val Ala Gly Thr Thr Gly Ala Arg His His
530 535 540

Thr Gln Leu Ile Phe Val Phe Leu Val Glu Thr Gly Phe His His Val
545 550 555 560

Gly Gln Asp Gly Leu Asp Leu Leu Asn Ser
565 570

<210> 116
<211> 135
<212> PRT
<213> Homo sapien

<400> 116

Met Asp Gly Arg Leu Asp Gly Trp Val Asp Gly Arg Gly Trp Pro Trp
1 5 10 15

169/383

Met Arg Ser Ala Leu His Thr Gln Thr Arg Trp Glu Arg Phe Val Glu
 20 25 30

His Asp Ser Leu Gln Gln Glu Tyr Met Cys Ala Tyr Leu Cys Gly Gln
 35 40 45

Lys Tyr Leu His Leu Gly Phe Gly Ala Ile Gln Glu Glu Met Ser Gln
 50 55 60

Lys Gln Leu Asn Gln Gly Leu Ser Thr Leu Trp Ile Leu Asn Leu Lys
 65 70 75 80

Met Gly Ala Gly Leu Cys Leu Lys Ala Leu Leu Ser His Leu Leu Gly
 85 90 95

Pro Trp Phe Asn Lys Ala Leu Ser Lys Leu Arg Lys Thr Thr Thr Thr
 100 105 110

Thr Gln Asn Lys Ser Ser Phe Phe Ser Ser Phe Leu Gly Lys Lys Ala
 115 120 125

Leu Phe Phe Arg Glu Arg Val
 130 135

<210> 117
 <211> 82
 <212> PRT
 <213> Homo sapien

<400> 117

Met Leu Leu Glu Arg Arg Ser Val Met Asp Val Val Ala Ala Glu Val
 1 5 10 15

Trp Gly Leu Thr Ala Gln Asn Leu Leu Leu Ser Cys Cys Gly Trp Met
 20 25 30

Glu Gly Trp Met Asp Gly Trp Met Ala Val Asp Gly Arg Gly Cys Ala
 35 40 45

Val Pro Cys Ile Pro Lys Pro Gly Gly Ser Val Leu Leu Ser Met Thr
 50 55 60

Ala Cys Ser Arg Asn Ile Cys Val Pro Ile Cys Val Asp Lys Asn Ile
 65 70 75 80

Tyr Thr

<210> 118
 <211> 146
 <212> PRT
 <213> Homo sapien

<400> 118

Asn His Tyr Arg Arg Ile Gly Ala Leu Asp Ala Ala Arg Ala Ala Gln
 1 5 10 15

Cys Asp Gly Cys Gly Arg Gly Arg Gly Leu Gly Pro Asp Cys Ser Glu
 20 25 30

Leu Ala Ala Val Leu Leu Arg Met Asp Gly Arg Leu Asp Gly Trp Val
 35 40 45

Asp Gly Arg Gly Trp Pro Trp Met Arg Ser Ala Leu His Thr Gln Thr
 50 55 60

Arg Trp Glu Arg Phe Val Glu His Asp Ser Leu Gln Gln Glu Tyr Met
 65 70 75 80

Cys Ala Tyr Leu Cys Gly Gln Lys Tyr Leu His Leu Gly Phe Gly Ala
 85 90 95

Ile Gln Glu Glu Met Ser Gln Lys Gln Leu Asn Gln Gly Leu Ser Thr
 100 105 110

Leu Trp Ile Leu Asn Leu Lys Met Gly Ala Gly Leu Cys Leu Lys Ala
 115 120 125

Leu Leu Ser His Leu Leu Gly Pro Trp Phe Asn Lys Ala Leu Ser Lys
 130 135 140

Leu Arg
 145

<210> 119
 <211> 614
 <212> PRT
 <213> Homo sapien

<400> 119

Met Asp Ser Pro Ser Pro Met Asp Pro His Met Ala Glu Gln Thr Phe
 1 5 10 15

Glu Gln Ala Ile Gln Ala Ala Ser Arg Ile Ile Arg Asn Glu Gln Phe

20	25	30
Ala Ile Arg Arg Phe Gln Ser Met Pro Val Arg Leu Leu Gly His Ser 35 40 45		
Pro Val Leu Arg Asn Ile Thr Asn Ser Gln Ala Pro Asp Gly Arg Arg 50 55 60		
Lys Ser Glu Ala Gly Ser Gly Ala Ala Ser Ser Ser Gly Glu Asp Lys 65 70 75 80		
Glu Asn Val Arg Phe Trp Lys Ala Gly Val Gly Ala Leu Arg Glu Glu 85 90 95		
Glu Gly Ala Cys Trp Gly Gly Ser Leu Ala Cys Glu Asp Pro Pro Leu 100 105 110		
Pro Ser Trp Leu Gln Asp Gly Phe Val Phe Lys Met Pro Trp Lys Pro 115 120 125		
Thr His Pro Ser Ser Thr His Ala Leu Ala Glu Trp Ala Ser Arg Arg 130 135 140		
Glu Ala Phe Ala Gln Arg Pro Ser Ser Ala Pro Asp Leu Met Cys Leu 145 150 155 160		
Ser Pro Asp Arg Lys Met Glu Val Glu Glu Leu Ser Pro Leu Ala Leu 165 170 175		
Gly Arg Phe Ser Leu Thr Pro Ala Glu Gly Asp Thr Glu Glu Asp Asp 180 185 190		
Gly Phe Val Asp Ile Leu Glu Ser Asp Leu Lys Val Asn Ser Leu Val 195 200 205		
Pro Pro Gly Pro Tyr Leu Pro Ile Pro Gly Phe Ala Gln Lys Lys Arg 210 215 220		
Ala Leu Ser Pro Val Trp Gln Asp His Asp Val Ile Pro Val Ser Glu 225 230 235 240		
Glu Glu Ser Glu Val Thr Glu Ser Gln Pro Asn Leu Trp Pro Met Arg 245 250 255		
Glu Glu Gln Val Ala Gly Ala Thr Val Glu Gly Gly Leu Gly Gly Arg 260 265 270		

Gly Ala Ser His Pro Asn Leu Glu Phe Ala Arg Glu Thr Gly Lys Ala
 275 280 285

Val Leu Glu Asp Ser Gly Thr Gly Gly Val Trp Pro Met Pro Val Gly
 290 295 300

Cys Asp Pro Val Leu Ala Asn Leu Ala Ser Asp Asp Asp Ala Val Pro
 305 310 315 320

Pro Gly Met Glu Ser Leu Ile Ser Ala Pro Leu Val Lys Thr Leu Glu
 325 330 335

Lys Glu Glu Glu Lys Asp Leu Val Met Tyr Ser Lys Cys Gln Arg Leu
 340 345 350

Phe Arg Ser Pro Ser Met Pro Cys Ser Val Ile Arg Pro Ile Leu Lys
 355 360 365

Arg Leu Glu Arg Pro Gln Asp Arg Asp Thr Pro Val Gln Asn Lys Arg
 370 375 380

Arg Arg Ser Val Thr Pro Pro Glu Glu Gln Gln Glu Ala Glu Glu Pro
 385 390 395 400

Lys Ala Arg Val Leu Arg Ser Lys Ser Leu Cys His Asp Glu Ile Glu
 405 410 415

Asn Leu Leu Asp Ser Asp His Arg Glu Leu Ile Gly Asp Tyr Ser Lys
 420 425 430

Ala Phe Leu Leu Gln Thr Val Asp Gly Lys His Gln Asp Leu Lys Tyr
 435 440 445

Ile Ser Pro Glu Thr Met Val Ala Leu Leu Thr Gly Lys Phe Ser Asn
 450 455 460

Ile Val Asp Lys Phe Val Ile Val Asp Cys Arg Tyr Pro Tyr Glu Tyr
 465 470 475 480

Glu Gly Gly His Ile Lys Thr Ala Val Asn Leu Pro Leu Glu Arg Asp
 485 490 495

Ala Glu Ser Phe Leu Leu Lys Ser Pro Ile Ala Pro Cys Ser Leu Asp
 500 505 510

Lys Arg Val Ile Leu Ile Phe His Cys Glu Phe Ser Ser Glu Arg Gly
515 520 525

Pro Arg Met Cys Arg Phe Ile Arg Glu Arg Asp Arg Ala Val Asn Asp
530 535 540

Tyr Pro Ser Leu Tyr Tyr Pro Glu Met Tyr Ile Leu Lys Gly Gly Tyr
545 550 555 560

Lys Glu Phe Phe Pro Gln His Pro Asn Phe Cys Glu Pro Gln Asp Tyr
565 570 575

Arg Pro Met Asn His Glu Ala Phe Lys Asp Glu Leu Lys Thr Phe Arg
580 585 590

Leu Lys Thr Arg Ser Trp Ala Gly Glu Arg Ser Arg Arg Glu Leu Cys
595 600 605

Ser Arg Leu Gln Asp Gln
610

<210> 120
<211> 413
<212> PRT
<213> Homo sapien

<400> 120

Leu Lys Gly Lys Gln Pro Cys Pro Thr Arg Pro Leu Pro Ser Tyr Pro
1 5 10 15

Trp Val Arg Pro Lys Glu Glu Ser Ser Glu Pro Leu Trp Gln Asp His
20 25 30

Asp Val Ile Pro Val Ser Glu Glu Glu Ser Glu Val Thr Glu Ser Gln
35 40 45

Pro Asn Leu Trp Pro Met Arg Glu Glu Gln Val Ala Gly Ala Thr Val
50 55 60

Glu Gly Gly Leu Gly Gly Arg Gly Ala Ser His Pro Asn Leu Glu Phe
65 70 75 80

Ala Arg Glu Thr Gly Lys Ala Val Leu Glu Asp Ser Gly Thr Gly Gly
85 90 95

Val Trp Pro Met Pro Val Gly Cys Asp Pro Val Leu Ala Asn Leu Ala

174/383

100	105	110
Ser Asp Asp Asp Ala Val Pro	Pro Gly Met Glu Ser Leu Ile Ser Ala	
115	120	125
Pro Leu Val Lys Thr Leu Glu Lys Glu Glu Glu Lys Asp Leu Val Met		
130	135	140
Tyr Ser Lys Cys Gln Arg Leu Phe Arg Ser Pro Ser Met Pro Cys Ser		
145	150	155
Val Ile Arg Pro Ile Leu Lys Arg Leu Glu Arg Pro Gln Asp Arg Asp		
165	170	175
Thr Pro Val Gln Asn Lys Arg Arg Arg Ser Val Thr Pro Pro Glu Glu		
180	185	190
Gln Gln Glu Ala Glu Glu Pro Lys Ala Arg Val Leu Arg Ser Lys Ser		
195	200	205
Leu Cys His Asp Glu Ile Glu Asn Leu Leu Asp Ser Asp His Arg Glu		
210	215	220
Leu Ile Gly Asp Tyr Ser Lys Ala Phe Leu Leu Gln Thr Val Asp Gly		
225	230	235
Lys His Gln Asp Leu Lys Tyr Ile Ser Pro Glu Thr Met Val Ala Leu		
245	250	255
Leu Thr Gly Lys Phe Ser Asn Ile Val Asp Lys Phe Val Ile Val Asp		
260	265	270
Cys Arg Tyr Pro Tyr Glu Tyr Glu Gly Gly His Ile Lys Thr Ala Val		
275	280	285
Asn Leu Pro Leu Glu Arg Asp Ala Glu Ser Phe Leu Leu Lys Ser Pro		
290	295	300
Ile Ala Pro Cys Ser Leu Asp Lys Arg Val Ile Leu Ile Phe His Cys		
305	310	315
Glu Phe Ser Ser Glu Arg Gly Pro Arg Met Cys Arg Phe Ile Arg Glu		
325	330	335
Arg Asp Arg Ala Val Asn Asp Tyr Pro Ser Leu Tyr Tyr Pro Glu Met		
340	345	350

Tyr Ile Leu Lys Gly Gly Tyr Lys Glu Phe Phe Pro Gln His Pro Asn
 355 360 365

Phe Cys Glu Pro Gln Asp Tyr Arg Pro Met Asn His Glu Ala Phe Lys
 370 375 380

Asp Glu Leu Lys Thr Phe Arg Leu Lys Thr Arg Ser Trp Ala Gly Glu
 385 390 395 400

Arg Ser Arg Arg Glu Leu Cys Ser Arg Leu Gln Asp Gln
 405 410

<210> 121

<211> 331

<212> PRT

<213> Homo sapien

<400> 121

Met Glu Asp Gly Val Leu Lys Glu Gly Phe Leu Val Lys Arg Gly His
 1 5 10 15

Ile Val His Asn Trp Lys Ala Arg Trp Phe Ile Leu Arg Gln Asn Thr
 20 25 30

Leu Val Tyr Tyr Lys Leu Glu Gly Gly Arg Arg Val Thr Pro Pro Lys
 35 40 45

Gly Arg Ile Leu Leu Asp Gly Cys Thr Ile Thr Cys Pro Cys Leu Glu
 50 55 60

Tyr Glu Asn Arg Pro Leu Leu Ile Lys Leu Lys Thr Gln Thr Ser Thr
 65 70 75 80

Glu Tyr Phe Leu Glu Ala Cys Ser Arg Glu Glu Arg Asp Ala Trp Ala
 85 90 95

Phe Glu Ile Thr Gly Ala Ile His Ala Gly Gln Pro Gly Lys Val Gln
 100 105 110

Gln Leu His Ser Leu Arg Asn Ser Phe Lys Leu Pro Pro His Ile Ser
 115 120 125

Leu His Arg Ile Val Asp Lys Met His Asp Ser Asn Thr Gly Ile Arg
 130 135 140

176/383

Ser Ser Pro Asn Met Glu Gln Gly Ser Thr Tyr Lys Lys Thr Phe Leu
145 150 155 160

Gly Ser Ser Leu Val Asp Trp Leu Ile Ser Asn Ser Phe Thr Ala Ser
165 170 175

Arg Leu Glu Ala Val Thr Leu Ala Ser Met Leu Met Glu Glu Asn Phe
180 185 190

Leu Arg Pro Val Gly Val Arg Ser Met Gly Ala Ile Arg Ser Gly Asp
195 200 205

Leu Ala Glu Gln Phe Leu Asp Asp Ser Thr Ala Leu Tyr Thr Phe Ala
210 215 220

Glu Ser Tyr Lys Lys Lys Ile Ser Pro Lys Glu Glu Ile Ser Leu Ser
225 230 235 240

Thr Val Glu Leu Ser Gly Thr Val Val Lys Gln Gly Tyr Leu Ala Lys
245 250 255

Gln Gly His Lys Arg Lys Asn Trp Lys Val Arg Arg Phe Val Leu Arg
260 265 270

Lys Asp Pro Ala Phe Leu His Tyr Tyr Asp Pro Ser Lys Glu Glu Asn
275 280 285

Arg Pro Val Gly Gly Phe Ser Leu Arg Gly Ser Leu Val Ser Ala Leu
290 295 300

Glu Asp Asn Gly Val Pro Thr Gly Lys Val Gln Leu Gln Pro Trp Pro
305 310 315 320

Glu Asp Leu Arg Gly Leu Pro Pro Ala Pro Gln
325 330

<210> 122

<211> 176

<212> PRT

<213> Homo sapien

<400> 122

Met Ser Ile Met Ser Tyr Asn Gly Gly Ala Val Met Ala Met Lys Gly
1 5 10 15

Lys Asn Cys Val Ala Ile Ala Ala Asp Arg Arg Phe Gly Ile Gln Ala
20 25 30

Gln Met Val Thr Thr Asp Phe Gln Lys Ile Phe Pro Met Gly Asp Arg
35 40 45

Leu Tyr Ile Gly Leu Ala Gly Leu Ala Thr Asp Val Gln Thr Val Ala
50 55 60

Gln Arg Leu Lys Phe Arg Leu Asn Leu Tyr Glu Leu Lys Glu Gly Arg
65 70 75 80

Gln Ile Lys Pro Tyr Thr Leu Met Ser Met Val Ala Asn Leu Leu Tyr
85 90 95

Glu Lys Arg Phe Gly Pro Tyr Tyr Thr Glu Pro Val Ile Ala Gly Leu
100 105 110

Asp Pro Lys Thr Phe Lys Pro Phe Ile Cys Ser Leu Asp Leu Ile Gly
115 120 125

Cys Pro Met Val Thr Asp Asp Phe Val Val Ser Gly Thr Cys Ala Glu
130 135 140

Gln Met Tyr Gly Met Cys Glu Ser Leu Trp Glu Pro Asn Met Val Arg
145 150 155 160

Trp Trp His Gly Glu Gly Leu Gly Ser Glu Leu Pro Thr Leu Gly His
165 170 175

<210> 123

<211> 158

<212> PRT

<213> Homo sapien

<400> 123

Met Ser Ile Met Ser Tyr Asn Gly Gly Ala Val Met Ala Met Lys Gly
1 5 10 15

Lys Asn Cys Val Ala Ile Ala Ala Asp Arg Arg Phe Gly Ile Gln Ala
20 25 30

Gln Met Val Thr Thr Asp Phe Gln Lys Ile Phe Pro Met Gly Asp Arg
35 40 45

Leu Tyr Ile Gly Leu Ala Gly Leu Ala Thr Asp Val Gln Thr Val Ala
50 55 60

178/383

Gln Arg Leu Lys Phe Arg Leu Asn Leu Tyr Glu Leu Lys Glu Gly Arg
65 70 75 80

Gln Ile Lys Pro Tyr Thr Leu Met Ser Met Val Ala Asn Leu Leu Tyr
85 90 95

Glu Lys Arg Phe Gly Pro Tyr Tyr Thr Glu Pro Val Ile Ala Gly Leu
100 105 110

Asp Pro Lys Thr Phe Lys Pro Phe Ile Cys Ser Leu Asp Leu Ile Gly
115 120 125

Cys Pro Met Val Thr Asp Asp Phe Val Val Ser Gly Thr Cys Ala Glu
130 135 140

Gln Met Tyr Leu Gly Arg Asp His Ala Lys Pro Asn Ser Ser
145 150 155

<210> 124
<211> 246
<212> PRT
<213> Homo sapien

<400> 124

Met Leu Phe Pro Gln Val Pro Pro Pro Arg Pro Gly Leu Ala Asp Pro
1 5 10 15

Pro Leu Pro Phe Pro Ser Ser Asn Leu Asn Lys Pro Tyr Leu Phe Ser
20 25 30

Val Leu Leu Gly Ala Trp Gln Leu Gly Asn Pro Gly Ser Arg Ser Gln
35 40 45

Lys Val Gly Val Ala Trp Val Glu Pro His Pro Val Tyr Ser Trp Lys
50 55 60

Glu Gly Ala Cys Ala Asp Ile Ala Leu Val Arg Leu Glu Arg Ser Ile
65 70 75 80

Gln Phe Ser Glu Arg Val Leu Pro Ile Cys Leu Pro Asp Ala Ser Ile
85 90 95

His Leu Pro Pro Asn Thr His Cys Trp Ile Ser Gly Trp Gly Ser Ile
100 105 110

Gln Asp Gly Val Pro Leu Pro His Pro Gln Thr Leu Gln Lys Leu Lys
115 120 125

Val Pro Ile Ile Asp Ser Glu Val Cys Ser His Leu Tyr Trp Arg Gly
130 135 140

Ala Gly Gln Gly Pro Ile Thr Glu Asp Met Leu Cys Ala Gly Tyr Leu
145 150 155 160

Glu Gly Glu Arg Asp Ala Cys Leu Gly Asp Ser Gly Gly Pro Leu Met
165 170 175

Cys Gln Val Asp Gly Ala Trp Leu Leu Ala Gly Ile Ile Ser Trp Gly
180 185 190

Glu Gly Cys Ala Glu Arg Asn Arg Pro Gly Val Tyr Ile Ser Leu Ser
195 200 205

Ala His Arg Ser Trp Val Glu Lys Ile Val Gln Gly Val Gln Leu Arg
210 215 220

Gly Arg Ala Gln Gly Gly Gly Ala Leu Arg Ala Pro Ser Gln Gly Ser
225 230 235 240

Gly Ala Ala Ala Arg Ser
245

<210> 125
<211> 273
<212> PRT
<213> Homo sapien

<400> 125

Met Arg Leu Trp Leu Gly Arg Asp Ala Glu Gly Thr Glu Leu Ser Arg
1 5 10 15

Arg His Asn Trp Thr Lys Pro Glu Pro Gln Ala Pro Val Ala Trp Glu
20 25 30

Arg Val Ala Pro Ser Asn Leu Pro Gln Gly His Pro Leu Pro Lys Ser
35 40 45

Phe Ser Ser Pro Pro Ser Pro Ser Asn Lys Arg Glu Glu Glu Glu Glu
50 55 60

Glu Phe Asn Phe Glu Val Ile Pro Pro Pro Pro Glu Phe Ser Asn Asp
65 70 75 80

180/383

Pro Glu Pro Pro Ala Pro Ala Leu Gln Tyr Leu Gly Arg Gln Ser Ser
85 90 95

Pro Pro Arg Asn Asn Tyr Ser Asp Leu Arg Gln Leu Pro Asn Ala Gly
100 105 110

Pro Gly Ala Pro Pro Ala Leu Gly Phe Ser Arg Phe Pro Ala Gly Ala
115 120 125

Arg Tyr Ala Gly Ala Gly Gly Leu Glu Arg Phe Ser Gly Gly Gly Arg
130 135 140

Ser Leu Ile Lys Lys Arg Leu Tyr Val Gly Glu Pro His Arg Gly Pro
145 150 155 160

Gly Leu Pro His Gly Gly Thr Gly Arg Ser Leu Ser Ser Pro Asn Cys
165 170 175

Phe Gly Pro Gln Pro Gly Gly Pro Glu Met Arg Arg Val Asn Ser Ala
180 185 190

Gly Arg Ala Pro Pro Gly Gly Leu His Ala Pro Arg Leu Ser Leu Glu
195 200 205

Gly Ala Ala Arg Gly Ala Ala Glu Ala Lys His Lys Ala Pro Gly Ser
210 215 220

Ala Asp Tyr Gly Phe Ala Pro Ala Ala Gly Arg Ser Pro Tyr Thr Thr
225 230 235 240

Thr Arg Tyr Gly Ser Pro Ile Asn Thr Phe Thr Val Arg Pro Gly Thr
245 250 255

Arg His Pro Ile Ser Tyr Val Cys Ser Gly Ala His Arg Lys Ala Thr
260 265 270

Ser

<210> 126

<211> 278

<212> PRT

<213> Homo sapien

<400> 126

Ser Ser Cys His Asn Leu Arg Leu Trp Leu Gly Arg Asp Ala Glu Gly
1 5 10 15

Thr Glu Leu Ser Arg Arg His Asn Trp Thr Lys Pro Glu Pro Gln Ala
20 25 30

Pro Val Ala Trp Glu Arg Val Ala Pro Ser Asn Leu Pro Gln Gly His
35 40 45

Pro Leu Pro Lys Ser Phe Ser Ser Pro Pro Ser Pro Ser Asn Lys Arg
50 55 60

Glu Glu Glu Glu Glu Glu Phe Asn Phe Glu Val Ile Pro Pro Pro Pro
65 70 75 80

Glu Phe Ser Asn Asp Pro Glu Pro Pro Ala Pro Ala Leu Gln Tyr Leu
85 90 95

Gly Arg Gln Ser Ser Pro Pro Arg Asn Asn Tyr Ser Asp Leu Arg Gln
100 105 110

Leu Pro Asn Ala Gly Pro Gly Ala Pro Pro Ala Leu Gly Phe Ser Arg
115 120 125

Phe Pro Ala Gly Ala Arg Tyr Ala Gly Ala Gly Gly Leu Glu Arg Phe
130 135 140

Ser Gly Gly Gly Arg Ser Leu Ile Lys Lys Arg Leu Tyr Val Gly Glu
145 150 155 160

Pro His Arg Gly Pro Gly Leu Pro His Gly Gly Thr Gly Arg Ser Leu
165 170 175

Ser Ser Pro Asn Cys Phe Gly Pro Gln Pro Gly Gly Pro Glu Met Arg
180 185 190

Arg Val Asn Ser Ala Gly Arg Ala Pro Pro Gly Gly Leu His Ala Pro
195 200 205

Arg Leu Ser Leu Glu Gly Ala Ala Arg Gly Ala Ala Glu Ala Lys His
210 215 220

Lys Ala Pro Gly Ser Ala Asp Tyr Gly Phe Ala Pro Ala Ala Gly Arg
225 230 235 240

Ser Pro Tyr Thr Thr Thr Arg Tyr Gly Ser Pro Ile Asn Thr Phe Thr
245 250 255

Val Arg Pro Gly Thr Arg His Pro Ile Ser Tyr Val Cys Ser Gly Ala
 260 265 270

His Arg Lys Ala Thr Ser
 275

<210> 127
 <211> 2306
 <212> PRT
 <213> Homo sapien

<400> 127

Met Ala Ala Leu Val Leu Glu Asp Gly Ser Val Leu Arg Gly Gln Pro
 1 5 10 15

Phe Gly Ala Ala Val Ser Thr Ala Gly Glu Val Val Phe Gln Thr Gly
 20 25 30

Met Val Gly Tyr Pro Glu Ala Leu Thr Asp Pro Ser Tyr Lys Ala Gln
 35 40 45

Ile Leu Val Leu Thr Tyr Pro Leu Ile Gly Asn Tyr Gly Ile Pro Pro
 50 55 60

Asp Glu Met Asp Glu Phe Gly Leu Cys Lys Trp Phe Glu Ser Ser Gly
 65 70 75 80

Ile His Val Ala Ala Leu Val Val Gly Glu Cys Cys Pro Thr Pro Ser
 85 90 95

His Trp Ser Ala Thr Arg Thr Leu His Glu Trp Leu Gln Gln His Gly
 100 105 110

Ile Pro Gly Leu Gln Gly Val Asp Thr Arg Glu Leu Thr Lys Lys Leu
 115 120 125

Arg Glu Gln Gly Ser Leu Leu Gly Lys Leu Val Gln Asn Gly Thr Glu
 130 135 140

Pro Ser Ser Leu Pro Phe Leu Asp Pro Asn Ala Arg Pro Leu Val Pro
 145 150 155 160

Glu Val Ser Ile Lys Thr Pro Arg Val Phe Asn Thr Gly Gly Ala Pro
 165 170 175

Arg Ile Leu Ala Leu Asp Cys Gly Leu Lys Tyr Asn Gln Ile Arg Cys

183/383

180	185	190
Leu Cys Gln Arg Gly Ala Glu Val Thr Val Val Pro Trp Asp His Ala 195 200 205		
Leu Asp Ser Gln Glu Tyr Glu Gly Leu Phe Leu Ser Asn Gly Pro Gly 210 215 220		
Asp Pro Ala Ser Tyr Pro Ser Val Val Ser Thr Leu Ser Arg Val Leu 225 230 235 240		
Ser Glu Pro Asn Pro Arg Pro Val Phe Gly Ile Cys Leu Gly His Gln 245 250 255		
Leu Leu Ala Leu Ala Ile Gly Ala Lys Thr Tyr Lys Met Arg Tyr Gly 260 265 270		
Asn Arg Gly His Asn Gln Pro Cys Leu Leu Val Gly Ser Gly Arg Cys 275 280 285		
Phe Leu Thr Ser Gln Asn His Gly Phe Ala Val Glu Thr Asp Ser Leu 290 295 300		
Pro Ala Asp Trp Ala Pro Leu Phe Thr Asn Ala Asn Asp Gly Ser Asn 305 310 315 320		
Glu Gly Ile Val His Asn Ser Leu Pro Phe Phe Ser Val Gln Phe His 325 330 335		
Pro Glu His Gln Ala Gly Pro Ser Asp Met Glu Leu Leu Phe Asp Ile 340 345 350		
Phe Leu Glu Thr Val Lys Glu Ala Thr Ala Gly Asn Pro Gly Gly Gln 355 360 365		
Thr Val Arg Glu Arg Leu Thr Glu Arg Leu Cys Pro Pro Gly Ile Pro 370 375 380		
Thr Pro Gly Ser Gly Leu Pro Pro Pro Arg Lys Val Leu Ile Leu Gly 385 390 395 400		
Ser Gly Gly Leu Ser Ile Gly Gln Ala Gly Glu Phe Asp Tyr Ser Gly 405 410 415		
Ser Gln Ala Ile Lys Ala Leu Lys Glu Glu Asn Ile Gln Thr Leu Leu 420 425 430		

Ile Asn Pro Asn Ile Ala Thr Val Gln Thr Ser Gln Gly Leu Ala Asp
 435 440 445

Lys Val Tyr Phe Leu Pro Ile Thr Pro His Tyr Val Thr Gln Val Ile
 450 455 460

Arg Asn Glu Arg Pro Asp Gly Val Leu Leu Thr Phe Gly Gly Gln Thr
 465 470 475 480

Ala Leu Asn Cys Gly Val Glu Leu Thr Lys Ala Gly Val Leu Ala Arg
 485 490 495

Tyr Gly Val Arg Val Leu Gly Thr Thr Val Glu Thr Ile Glu Leu Thr
 500 505 510

Glu Asp Arg Arg Ala Phe Ala Ala Arg Met Ala Glu Ile Gly Glu His
 515 520 525

Val Ala Pro Ser Glu Ala Gly Asn Ser Leu Glu Gln Ala Gln Ala Ala
 530 535 540

Ala Glu Arg Leu Gly Tyr Pro Val Leu Val Arg Ala Ala Phe Ala Val
 545 550 555 560

Gly Gly Leu Gly Ser Gly Phe Ala Ser Asn Arg Glu Glu Leu Ser Ala
 565 570 575

Leu Val Ala Pro Ala Phe Ala His Thr Ser Gln Val Leu Val Asp Lys
 580 585 590

Ser Leu Lys Gly Trp Lys Glu Ile Glu Tyr Glu Val Val Arg Asp Ala
 595 600 605

Tyr Gly Asn Cys Val Thr Val Cys Asn Met Glu Asn Leu Asp Pro Leu
 610 615 620

Gly Ile His Thr Gly Glu Ser Ile Val Val Ala Pro Ser Gln Thr Leu
 625 630 635 640

Asn Asp Arg Glu Tyr Gln Leu Leu Arg Gln Thr Ala Ile Lys Val Thr
 645 650 655

Gln His Leu Gly Ile Val Gly Glu Cys Asn Val Gln Tyr Ala Leu Asn
 660 665 670

Pro Glu Ser Glu Gln Tyr Tyr Ile Ile Glu Val Asn Ala Arg Leu Ser
675 680 685

Arg Ser Ser Ala Leu Ala Ser Lys Ala Thr Gly Tyr Pro Leu Ala Tyr
690 695 700

Val Ala Ala Lys Leu Ala Leu Gly Ile Pro Leu Pro Glu Leu Arg Asn
705 710 715 720

Ser Val Thr Gly Gly Thr Ala Ala Phe Glu Pro Ser Val Asp Tyr Cys
725 730 735

Val Val Lys Ile Pro Arg Trp Asp Leu Ser Lys Phe Leu Arg Val Ser
740 745 750

Thr Lys Ile Gly Ser Cys Met Lys Ser Val Gly Glu Val Met Gly Ile
755 760 765

Gly Arg Ser Phe Glu Glu Ala Phe Gln Lys Ala Leu Arg Met Val Asp
770 775 780

Glu Asn Cys Val Gly Phe Asp His Thr Val Lys Pro Val Ser Asp Met
785 790 795 800

Glu Leu Glu Thr Pro Thr Asp Lys Arg Ile Phe Val Val Ala Ala Ala
805 810 815

Leu Trp Ala Gly Tyr Ser Val Asp Arg Leu Tyr Glu Leu Thr Arg Ile
820 825 830

Asp Arg Trp Phe Leu His Arg Met Lys Arg Ile Ile Ala His Ala Gln
835 840 845

Leu Leu Glu Gln His Arg Gly Gln Pro Leu Pro Pro Asp Leu Leu Gln
850 855 860

Gln Ala Lys Cys Leu Gly Phe Ser Asp Lys Gln Ile Ala Leu Ala Val
865 870 875 880

Leu Ser Thr Glu Leu Ala Val Arg Lys Leu Arg Gln Glu Leu Gly Ile
885 890 895

Cys Pro Ala Val Lys Gln Ile Asp Thr Val Ala Ala Glu Trp Pro Ala
900 905 910

Gln Thr Asn Tyr Leu Tyr Leu Thr Tyr Trp Gly Thr Thr His Asp Leu
 915 920 925

Thr Phe Arg Thr Pro His Val Leu Val Leu Gly Ser Gly Val Tyr Arg
 930 935 940

Ile Gly Ser Ser Val Glu Phe Asp Trp Cys Ala Val Gly Cys Ile Gln
 945 950 955 960

Gln Leu Arg Lys Met Gly Tyr Lys Thr Ile Met Val Asn Tyr Asn Pro
 965 970 975

Glu Thr Val Ser Thr Asp Tyr Asp Met Cys Asp Arg Leu Tyr Phe Asp
 980 985 990

Glu Ile Ser Phe Glu Val Val Met Asp Ile Tyr Glu Leu Glu Asn Pro
 995 1000 1005

Glu Gly Val Ile Leu Ser Met Gly Gly Gln Leu Pro Asn Asn Met
 1010 1015 1020

Ala Met Ala Leu His Arg Gln Gln Cys Arg Val Leu Gly Thr Ser
 1025 1030 1035

Pro Glu Ala Ile Asp Ser Ala Glu Asn Arg Phe Lys Phe Ser Arg
 1040 1045 1050

Leu Leu Asp Thr Ile Gly Ile Ser Gln Pro Gln Trp Arg Glu Leu
 1055 1060 1065

Ser Asp Leu Glu Ser Ala Arg Gln Phe Cys Gln Thr Val Gly Tyr
 1070 1075 1080

Pro Cys Val Val Arg Pro Ser Tyr Val Leu Ser Gly Ala Ala Met
 1085 1090 1095

Asn Val Ala Tyr Thr Asp Gly Asp Leu Glu Arg Phe Leu Ser Ser
 1100 1105 1110

Ala Ala Ala Val Ser Lys Glu His Pro Val Val Ile Ser Lys Phe
 1115 1120 1125

Ile Gln Glu Ala Lys Glu Ile Asp Val Asp Ala Val Ala Ser Asp
 1130 1135 1140

Gly Val Val Ala Ala Ile Ala Ile Ser Glu His Val Glu Asn Ala

1145	1150	1155
Gly Val His Ser Gly Asp Ala Thr Leu Val Thr Pro Pro Gln Asp 1160 1165 1170		
Ile Thr Ala Lys Thr Leu Glu Arg Ile Lys Ala Ile Val His Ala 1175 1180 1185		
Val Gly Gln Glu Leu Gln Val Thr Gly Pro Phe Asn Leu Gln Leu 1190 1195 1200		
Ile Ala Lys Asp Asp Gln Leu Lys Val Ile Glu Cys Asn Val Arg 1205 1210 1215		
Val Ser Arg Ser Phe Pro Phe Val Ser Lys Thr Leu Gly Val Asp 1220 1225 1230		
Leu Val Ala Leu Ala Thr Arg Val Ile Met Gly Glu Glu Val Glu 1235 1240 1245		
Pro Val Gly Leu Met Thr Gly Ser Gly Val Val Gly Val Lys Val 1250 1255 1260		
Pro Gln Phe Ser Phe Ser Arg Leu Ala Gly Ala Asp Val Val Leu 1265 1270 1275		
Gly Val Glu Met Thr Ser Thr Gly Glu Val Ala Gly Phe Gly Glu 1280 1285 1290		
Ser Arg Cys Glu Ala Tyr Leu Lys Ala Met Leu Ser Thr Gly Phe 1295 1300 1305		
Lys Ile Pro Lys Lys Asn Ile Leu Leu Thr Ile Gly Ser Tyr Lys 1310 1315 1320		
Asn Lys Ser Glu Leu Leu Pro Thr Val Arg Leu Leu Glu Ser Leu 1325 1330 1335		
Gly Tyr Ser Leu Tyr Ala Ser Leu Gly Thr Ala Asp Phe Tyr Thr 1340 1345 1350		
Glu His Gly Val Lys Val Thr Ala Val Asp Trp His Phe Glu Glu 1355 1360 1365		
Ala Val Asp Gly Glu Cys Pro Pro Gln Arg Ser Ile Leu Glu Gln 1370 1375 1380		

Leu Ala 1385	Glu Lys Asn Phe	Glu 1390	Leu Val Ile Asn	Leu 1395	Ser Met Arg
Gly Ala 1400	Gly Gly Arg Arg	Leu 1405	Ser Ser Phe Val	Thr 1410	Lys Gly Tyr
Arg Thr 1415	Arg Arg Leu Ala	Ala 1420	Asp Phe Ser Val	Pro 1425	Leu Ile Ile
Asp Ile 1430	Lys Cys Thr Lys	Leu 1435	Phe Val Glu Ala	Leu 1440	Gly Gln Ile
Gly Pro 1445	Ala Pro Pro Leu	Lys 1450	Val His Val Asp	Cys 1455	Met Thr Ser
Gln Lys 1460	Leu Val Arg Leu	Pro 1465	Gly Leu Ile Asp	Val 1470	His Val His
Leu Arg 1475	Glu Pro Gly Gly	Thr 1480	His Lys Glu Asp	Phe 1485	Ala Ser Gly
Thr Ala 1490	Ala Ala Leu Ala	Gly 1495	Gly Ile Thr Met	Val 1500	Cys Ala Met
Pro Asn 1505	Thr Arg Pro Pro	Ile 1510	Ile Asp Ala Pro	Ala 1515	Leu Ala Leu
Ala Gln 1520	Lys Leu Ala Glu	Ala 1525	Gly Ala Arg Cys	Asp 1530	Phe Ala Leu
Phe Leu 1535	Gly Ala Ser Ser	Glu 1540	Asn Ala Gly Thr	Leu 1545	Gly Thr Val
Ala Gly 1550	Ser Ala Ala Gly	Leu 1555	Lys Leu Tyr Leu	Asn 1560	Glu Thr Phe
Ser Glu 1565	Leu Arg Leu Asp	Ser 1570	Val Val Gln Trp	Met 1575	Glu His Phe
Glu Thr 1580	Trp Pro Ser His	Leu 1585	Pro Ile Val Ala	His 1590	Ala Glu Gln
Gln Thr 1595	Val Ala Ala Val	Leu 1600	Met Val Ala Gln	Leu 1605	Thr Gln Arg

Ser Val	His Ile Cys His	Val	Ala Arg Lys Glu Glu	Val Arg Val
1610		1615		1620
His Leu	Arg Ser Cys Cys	Pro	Cys Cys Phe Pro Ser	Asn Thr Lys
1625		1630		1635
Gly Gln	Val Val Leu Arg	Gly	Arg Arg Gln Gln Glu	Glu Ser Leu
1640		1645		1650
Glu Thr	Ala Gly Gly Gly	Ser	Arg Ala Ser Thr Leu	Ala Gly Leu
1655		1660		1665
His His	His Phe Phe Glu	Gln	Gly Cys Trp Pro Leu	Gly Leu Cys
1670		1675		1680
Val Gly	Gln Gly Ile Trp	Val	Val Pro Leu Leu Asp	Leu Pro Ile
1685		1690		1695
Val Pro	Gln Ile Leu Leu	Ile	Lys Ala Ala Lys Ala	Arg Gly Leu
1700		1705		1710
Pro Val	Thr Cys Glu Val	Ala	Pro His His Leu Phe	Leu Ser His
1715		1720		1725
Asp Asp	Leu Glu Arg Leu	Gly	Pro Gly Lys Gly Glu	Val Arg Pro
1730		1735		1740
Glu Leu	Gly Ser Arg Gln	Asp	Val Glu Ala Leu Trp	Glu Asn Met
1745		1750		1755
Ala Val	Ile Asp Cys Phe	Ala	Ser Asp His Ala Pro	His Thr Leu
1760		1765		1770
Glu Glu	Lys Cys Gly Ser	Arg	Pro Pro Pro Gly Phe	Pro Gly Leu
1775		1780		1785
Glu Thr	Met Leu Pro Leu	Leu	Leu Thr Ala Val Ser	Glu Gly Arg
1790		1795		1800
Leu Ser	Leu Asp Asp Leu	Leu	Gln Arg Leu His His	Asn Pro Arg
1805		1810		1815
Arg Ile	Phe His Leu Pro	Pro	Gln Glu Asp Thr Tyr	Val Glu Val
1820		1825		1830

190/383

Asp	Leu	Glu	His	Glu	Trp	Thr	Ile	Pro	Ser	His	Met	Pro	Phe	Ser
1835						1840					1845			
Lys	Ala	His	Trp	Thr	Pro	Phe	Glu	Gly	Gln	Lys	Val	Lys	Gly	Thr
1850						1855					1860			
Val	Arg	Arg	Val	Val	Leu	Arg	Gly	Glu	Val	Ala	Tyr	Ile	Asp	Gly
1865						1870					1875			
Gln	Val	Leu	Val	Pro	Pro	Gly	Tyr	Gly	Gln	Asp	Val	Arg	Lys	Trp
1880						1885					1890			
Pro	Gln	Gly	Ala	Val	Pro	Gln	Leu	Pro	Pro	Ser	Ala	Pro	Ala	Thr
1895						1900					1905			
Ser	Glu	Met	Thr	Thr	Thr	Pro	Glu	Arg	Pro	Arg	Arg	Gly	Ile	Pro
1910						1915					1920			
Gly	Leu	Pro	Asp	Gly	Arg	Phe	His	Leu	Pro	Pro	Arg	Ile	His	Arg
1925						1930					1935			
Ala	Ser	Asp	Pro	Gly	Leu	Pro	Ala	Glu	Glu	Pro	Lys	Glu	Lys	Ser
1940						1945					1950			
Ser	Arg	Lys	Val	Ala	Glu	Pro	Glu	Leu	Met	Gly	Thr	Pro	Asp	Gly
1955						1960					1965			
Thr	Cys	Tyr	Pro	Pro	Pro	Pro	Val	Pro	Arg	Gln	Ala	Ser	Pro	Gln
1970						1975					1980			
Asn	Leu	Gly	Thr	Pro	Gly	Leu	Leu	His	Pro	Gln	Thr	Ser	Pro	Leu
1985						1990					1995			
Leu	His	Ser	Leu	Val	Gly	Gln	His	Ile	Leu	Ser	Val	Gln	Gln	Phe
2000						2005					2010			
Thr	Lys	Asp	Gln	Met	Ser	His	Leu	Phe	Asn	Val	Ala	His	Thr	Leu
2015						2020					2025			
Arg	Met	Met	Val	Gln	Lys	Glu	Arg	Ser	Leu	Asp	Ile	Leu	Lys	Gly
2030						2035					2040			
Lys	Val	Met	Ala	Ser	Met	Phe	Tyr	Glu	Val	Ser	Thr	Arg	Thr	Ser
2045						2050					2055			
Ser	Ser	Phe	Ala	Ala	Ala	Met	Ala	Arg	Leu	Gly	Gly	Ala	Val	Leu

2060	2065	2070
Ser Phe Ser Glu Ala Thr Ser Ser Val Gln Lys Gly Glu Ser Leu		
2075	2080	2085
Ala Asp Ser Val Gln Thr Met Ser Cys Tyr Ala Asp Val Val Val		
2090	2095	2100
Leu Arg His Pro Gln Pro Gly Ala Val Glu Leu Ala Ala Lys His		
2105	2110	2115
Cys Arg Arg Pro Val Ile Asn Ala Gly Asp Gly Val Gly Glu His		
2120	2125	2130
Pro Thr Gln Ala Leu Leu Asp Ile Phe Thr Ile Arg Glu Glu Leu		
2135	2140	2145
Gly Thr Val Asn Gly Met Thr Ile Thr Met Val Gly Asp Leu Lys		
2150	2155	2160
His Gly Arg Thr Val His Ser Leu Ala Cys Leu Leu Thr Gln Tyr		
2165	2170	2175
Arg Val Ser Leu Arg Tyr Val Ala Pro Pro Ser Leu Arg Met Pro		
2180	2185	2190
Pro Thr Val Arg Ala Phe Val Ala Ser Arg Gly Thr Lys Gln Glu		
2195	2200	2205
Glu Phe Glu Ser Ile Glu Glu Ala Leu Pro Asp Thr Asp Val Leu		
2210	2215	2220
Tyr Met Thr Arg Ile Gln Lys Glu Arg Phe Gly Ser Thr Gln Glu		
2225	2230	2235
Tyr Glu Ala Cys Phe Gly Gln Phe Ile Leu Thr Pro His Ile Met		
2240	2245	2250
Thr Arg Ala Lys Lys Lys Met Val Val Met His Pro Met Pro Arg		
2255	2260	2265
Val Asn Glu Ile Ser Val Glu Val Asp Ser Asp Pro Arg Ala Ala		
2270	2275	2280
Tyr Phe Arg Gln Ala Glu Asn Gly Met Tyr Ile Arg Met Ala Leu		
2285	2290	2295

Leu Ala Thr Val Leu Gly Arg Phe
2300 2305

<210> 128
<211> 1651
<212> PRT
<213> Homo sapien

<400> 128

Pro Pro Pro Leu Ser Ser Leu Pro Met Ala Ala Leu Val Leu Glu Asp
1 5 10 15

Gly Ser Val Leu Arg Gly Gln Pro Phe Gly Ala Ala Val Ser Thr Ala
20 25 30

Gly Glu Val Val Phe Gln Thr Gly Met Val Gly Tyr Pro Glu Ala Leu
35 40 45

Thr Asp Pro Ser Tyr Lys Ala Gln Ile Leu Val Leu Thr Tyr Pro Leu
50 55 60

Ile Gly Asn Tyr Gly Ile Pro Pro Asp Glu Met Asp Glu Phe Gly Leu
65 70 75 80

Cys Lys Trp Phe Glu Ser Ser Gly Ile His Val Ala Ala Leu Val Val
85 90 95

Gly Glu Cys Cys Pro Thr Pro Ser His Trp Ser Ala Thr Arg Thr Leu
100 105 110

His Glu Trp Leu Gln Gln His Gly Ile Pro Gly Leu Gln Gly Val Asp
115 120 125

Thr Arg Glu Leu Thr Lys Lys Leu Arg Glu Gln Gly Ser Leu Leu Gly
130 135 140

Lys Leu Val Gln Asn Gly Thr Glu Pro Ser Ser Leu Pro Phe Leu Asp
145 150 155 160

Pro Asn Ala Arg Pro Leu Val Pro Glu Val Ser Ile Lys Thr Pro Arg
165 170 175

Val Phe Asn Thr Gly Gly Ala Pro Arg Ile Leu Ala Leu Asp Cys Gly
180 185 190

Leu Lys Tyr Asn Gln Ile Arg Cys Leu Cys Gln Arg Gly Ala Glu Val
 195 200 205

Thr Val Val Pro Trp Asp His Ala Leu Asp Ser Gln Glu Tyr Glu Gly
 210 215 220

Leu Phe Leu Ser Asn Gly Pro Gly Asp Pro Ala Ser Tyr Pro Ser Val
 225 230 235 240

Val Ser Thr Leu Ser Arg Val Leu Ser Glu Pro Asn Pro Arg Pro Val
 245 250 255

Phe Gly Ile Cys Leu Gly His Gln Leu Leu Ala Leu Ala Ile Gly Ala
 260 265 270

Lys Thr Tyr Lys Met Arg Tyr Gly Asn Arg Gly His Asn Gln Pro Cys
 275 280 285

Leu Leu Val Gly Ser Gly Arg Cys Phe Leu Thr Ser Gln Asn His Gly
 290 295 300

Phe Ala Val Glu Thr Asp Ser Leu Pro Ala Asp Trp Ala Pro Leu Phe
 305 310 315 320

Thr Asn Ala Asn Asp Gly Ser Asn Glu Gly Ile Val His Asn Ser Leu
 325 330 335

Pro Phe Phe Ser Val Gln Phe His Pro Glu His Gln Ala Gly Pro Ser
 340 345 350

Asp Met Glu Leu Leu Phe Asp Ile Phe Leu Glu Thr Val Lys Glu Ala
 355 360 365

Thr Ala Gly Asn Pro Gly Gly Gln Thr Val Arg Glu Arg Leu Thr Glu
 370 375 380

Arg Leu Cys Pro Pro Gly Ile Pro Thr Pro Gly Ser Gly Leu Pro Pro
 385 390 395 400

Pro Arg Lys Val Leu Ile Leu Gly Ser Gly Gly Leu Ser Ile Gly Gln
 405 410 415

Ala Gly Glu Phe Asp Tyr Ser Gly Ser Gln Ala Ile Lys Ala Leu Lys
 420 425 430

Glu Glu Asn Ile Gln Thr Leu Leu Ile Asn Pro Asn Ile Ala Thr Val

194/383

435	440	445
Gln Thr Ser Gln Gly Leu Ala Asp Lys Val Tyr Phe Leu Pro Ile Thr		
450	455	460
Pro His Tyr Val Thr Gln Val Ile Arg Asn Glu Arg Pro Asp Gly Val		
465	470	475
Leu Leu Thr Phe Gly Gly Gln Thr Ala Leu Asn Cys Gly Val Glu Leu		
485	490	495
Thr Lys Ala Gly Val Leu Ala Arg Tyr Gly Val Arg Val Leu Gly Thr		
500	505	510
Thr Val Glu Thr Ile Glu Leu Thr Glu Asp Arg Arg Ala Phe Ala Ala		
515	520	525
Arg Met Ala Glu Ile Gly Glu His Val Ala Pro Ser Glu Ala Gly Asn		
530	535	540
Ser Leu Glu Gln Ala Gln Ala Ala Ala Glu Arg Leu Gly Tyr Pro Val		
545	550	555
Leu Val Arg Ala Ala Phe Ala Val Gly Gly Leu Gly Ser Gly Phe Ala		
565	570	575
Ser Asn Arg Glu Glu Leu Ser Ala Leu Val Ala Pro Ala Phe Ala His		
580	585	590
Thr Ser Gln Val Leu Val Asp Lys Ser Leu Lys Gly Trp Lys Glu Ile		
595	600	605
Glu Tyr Glu Val Val Arg Asp Ala Tyr Gly Asn Cys Val Thr Val Cys		
610	615	620
Asn Met Glu Asn Leu Asp Pro Leu Gly Ile His Thr Gly Glu Ser Ile		
625	630	635
Val Val Ala Pro Ser Gln Thr Leu Asn Asp Arg Glu Tyr Gln Leu Leu		
645	650	655
Arg Gln Thr Ala Ile Lys Val Thr Gln His Leu Gly Ile Val Gly Glu		
660	665	670
Cys Asn Val Gln Tyr Ala Leu Asn Pro Glu Ser Glu Gln Tyr Tyr Ile		
675	680	685

Ile Glu Val Asn Ala Arg Leu Ser Arg Ser Ser Ala Leu Ala Ser Lys
 690 695 700

Ala Thr Gly Tyr Pro Leu Ala Tyr Val Ala Ala Lys Leu Ala Leu Gly
 705 710 715 720

Ile Pro Leu Pro Glu Leu Arg Asn Ser Val Thr Gly Gly Thr Ala Ala
 725 730 735

Phe Glu Pro Ser Val Asp Tyr Cys Val Val Lys Ile Pro Arg Trp Asp
 740 745 750

Leu Ser Lys Phe Leu Arg Val Ser Thr Lys Ile Gly Ser Cys Met Lys
 755 760 765

Ser Val Gly Glu Val Met Gly Ile Gly Arg Ser Phe Glu Glu Ala Phe
 770 775 780

Gln Lys Ala Leu Arg Met Val Asp Glu Asn Cys Val Gly Phe Asp His
 785 790 795 800

Thr Val Lys Pro Val Ser Asp Met Glu Leu Glu Thr Pro Thr Asp Lys
 805 810 815

Arg Ile Phe Val Val Ala Ala Ala Leu Trp Ala Gly Tyr Ser Val Asp
 820 825 830

Arg Leu Tyr Glu Leu Thr Arg Ile Asp Arg Trp Phe Leu His Arg Met
 835 840 845

Lys Arg Ile Ile Ala His Ala Gln Leu Leu Glu Gln His Arg Gly Gln
 850 855 860

Pro Leu Pro Pro Asp Leu Leu Gln Gln Ala Lys Cys Leu Gly Phe Ser
 865 870 875 880

Asp Lys Gln Ile Ala Leu Ala Val Leu Ser Thr Glu Leu Ala Val Arg
 885 890 895

Lys Leu Arg Gln Glu Leu Gly Ile Cys Pro Ala Val Lys Gln Ile Asp
 900 905 910

Thr Val Ala Ala Glu Trp Pro Ala Gln Thr Asn Tyr Leu Tyr Leu Thr
 915 920 925

Tyr Trp Gly Thr Thr His Asp Leu Thr Phe Arg Thr Pro His Val Leu
 930 935 940

Val Leu Gly Ser Gly Val Tyr Arg Ile Gly Ser Ser Val Glu Phe Asp
 945 950 955 960

Trp Cys Ala Val Gly Cys Ile Gln Gln Leu Arg Lys Met Gly Tyr Lys
 965 970 975

Thr Ile Met Val Asn Tyr Asn Pro Glu Thr Val Ser Thr Asp Tyr Asp
 980 985 990

Met Cys Asp Arg Leu Tyr Phe Asp Glu Ile Ser Phe Glu Val Val Met
 995 1000 1005

Asp Ile Tyr Glu Leu Glu Asn Pro Glu Gly Val Ile Leu Ser Met
 1010 1015 1020

Gly Gly Gln Leu Pro Asn Asn Met Ala Met Ala Leu His Arg Gln
 1025 1030 1035

Gln Cys Arg Val Leu Gly Thr Ser Pro Glu Ala Ile Asp Ser Ala
 1040 1045 1050

Glu Asn Arg Phe Lys Phe Ser Arg Leu Leu Asp Thr Ile Gly Ile
 1055 1060 1065

Ser Gln Pro Gln Trp Arg Glu Leu Ser Asp Leu Glu Ser Ala Arg
 1070 1075 1080

Gln Phe Cys Gln Thr Val Gly Tyr Pro Cys Val Val Arg Pro Ser
 1085 1090 1095

Tyr Val Leu Ser Gly Ala Ala Met Asn Val Ala Tyr Thr Asp Gly
 1100 1105 1110

Asp Leu Glu Arg Phe Leu Ser Ser Ala Ala Ala Val Ser Lys Glu
 1115 1120 1125

His Pro Val Val Ile Ser Lys Phe Ile Gln Glu Ala Lys Glu Ile
 1130 1135 1140

Asp Val Asp Ala Val Ala Ser Asp Gly Val Val Ala Ala Ile Ala
 1145 1150 1155

197/383

Ile Ser	Glu His	Val Glu	Asn Ala	Gly Val	His Ser	Gly Asp	Ala
1160			1165			1170	
Thr Leu	Val Thr	Pro Pro	Gln Asp	Ile Thr	Ala Lys	Thr Leu	Glu
1175			1180			1185	
Arg Ile	Lys Ala	Ile Val	His Ala	Val Gly	Gln Glu	Leu Gln	Val
1190			1195			1200	
Thr Gly	Pro Phe	Asn Leu	Gln Leu	Ile Ala	Lys Asp	Asp Gln	Leu
1205			1210			1215	
Lys Val	Ile Glu	Cys Asn	Val Arg	Val Ser	Arg Ser	Phe Pro	Phe
1220			1225			1230	
Val Ser	Lys Thr	Leu Gly	Val Asp	Leu Val	Ala Leu	Ala Thr	Arg
1235			1240			1245	
Val Ile	Met Gly	Glu Glu	Val Glu	Pro Val	Gly Leu	Met Thr	Gly
1250			1255			1260	
Ser Gly	Val Val	Gly Val	Lys Val	Pro Gln	Phe Ser	Phe Ser	Arg
1265			1270			1275	
Leu Ala	Gly Ala	Asp Val	Val Leu	Gly Val	Glu Met	Thr Ser	Thr
1280			1285			1290	
Gly Glu	Val Ala	Gly Phe	Gly Glu	Ser Arg	Cys Glu	Ala Tyr	Leu
1295			1300			1305	
Lys Ala	Met Leu	Ser Thr	Gly Phe	Lys Ile	Pro Lys	Lys Asn	Ile
1310			1315			1320	
Leu Leu	Thr Ile	Gly Ser	Tyr Lys	Asn Lys	Ser Glu	Leu Leu	Pro
1325			1330			1335	
Thr Val	Arg Leu	Leu Glu	Ser Leu	Gly Tyr	Ser Leu	Tyr Ala	Ser
1340			1345			1350	
Leu Gly	Thr Ala	Asp Phe	Tyr Thr	Glu His	Gly Val	Lys Val	Thr
1355			1360			1365	
Ala Val	Asp Trp	His Phe	Glu Glu	Ala Val	Asp Gly	Glu Cys	Pro
1370			1375			1380	
Pro Gln	Arg Ser	Ile Leu	Glu Gln	Leu Ala	Glu Lys	Asn Phe	Glu

1385	1390	1395
Leu Val Ile Asn Leu Ser Met Arg Gly Ala Gly Gly Arg Arg Leu		
1400	1405	1410
Ser Ser Phe Val Thr Lys Gly Tyr Arg Thr Arg Arg Leu Ala Ala		
1415	1420	1425
Asp Phe Ser Val Pro Leu Ile Ile Asp Ile Lys Cys Thr Lys Leu		
1430	1435	1440
Phe Val Glu Ala Leu Gly Gln Ile Gly Pro Ala Pro Pro Leu Lys		
1445	1450	1455
Val His Val Asp Cys Met Thr Ser Gln Lys Leu Val Arg Leu Pro		
1460	1465	1470
Gly Leu Ile Asp Val His Val His Leu Arg Glu Pro Gly Gly Thr		
1475	1480	1485
His Lys Glu Asp Phe Ala Ser Gly Thr Ala Ala Ala Leu Ala Gly		
1490	1495	1500
Gly Ile Thr Met Val Cys Ala Met Pro Asn Thr Arg Pro Pro Ile		
1505	1510	1515
Ile Asp Ala Pro Ala Leu Ala Leu Ala Gln Lys Leu Ala Glu Ala		
1520	1525	1530
Gly Ala Arg Cys Asp Phe Ala Leu Phe Leu Gly Ala Ser Ser Glu		
1535	1540	1545
Asn Ala Gly Thr Leu Gly Thr Val Ala Gly Ser Ala Ala Gly Leu		
1550	1555	1560
Lys Leu Tyr Leu Asn Glu Thr Phe Ser Glu Leu Arg Leu Asp Ser		
1565	1570	1575
Val Val Gln Trp Met Glu His Phe Glu Thr Trp Pro Ser His Leu		
1580	1585	1590
Pro Ile Val Ala His Ala Glu Gln Gln Thr Val Ala Ala Val Leu		
1595	1600	1605
Met Val Ala Gln Leu Thr Gln Arg Ser Val His Ile Cys His Val		
1610	1615	1620

Ala Arg Lys Glu Glu Val Arg Val His Leu Arg Ser Cys Cys Pro
 1625 1630 1635

Cys Cys Phe Pro Ser Asn Thr Lys Gly Gln Gly Ser Pro
 1640 1645 1650

<210> 129
 <211> 2242
 <212> PRT
 <213> Homo sapien

<400> 129

Met Ala Ala Leu Val Leu Glu Asp Gly Ser Val Leu Arg Gly Gln Pro
 1 5 10 15

Phe Gly Ala Ala Val Ser Thr Ala Gly Glu Val Val Phe Gln Thr Gly
 20 25 30

Met Val Gly Tyr Pro Glu Ala Leu Thr Asp Pro Ser Tyr Lys Ala Gln
 35 40 45

Ile Leu Val Leu Thr Tyr Pro Leu Ile Gly Asn Tyr Gly Ile Pro Pro
 50 55 60

Asp Glu Met Asp Glu Phe Gly Leu Cys Lys Trp Phe Glu Ser Ser Gly
 65 70 75 80

Ile His Val Ala Ala Leu Val Val Gly Glu Cys Cys Pro Thr Pro Ser
 85 90 95

His Trp Ser Ala Thr Arg Thr Leu His Glu Trp Leu Gln Gln His Gly
 100 105 110

Ile Pro Gly Leu Gln Gly Val Asp Thr Arg Glu Leu Thr Lys Lys Leu
 115 120 125

Arg Glu Gln Gly Ser Leu Leu Gly Lys Leu Val Gln Asn Gly Thr Glu
 130 135 140

Pro Ser Ser Leu Pro Phe Leu Asp Pro Asn Ala Arg Pro Leu Val Pro
 145 150 155 160

Glu Val Ser Ile Lys Thr Pro Arg Val Phe Asn Thr Gly Gly Ala Pro
 165 170 175

200/383

Arg Ile Leu Ala Leu Asp Cys Gly Leu Lys Tyr Asn Gln Ile Arg Cys
 180 185 190

Leu Cys Gln Arg Gly Ala Glu Val Thr Val Val Pro Trp Asp His Ala
 195 200 205

Leu Asp Ser Gln Glu Tyr Glu Gly Leu Phe Leu Ser Asn Gly Pro Gly
 210 215 220

Asp Pro Ala Ser Tyr Pro Ser Val Val Ser Thr Leu Ser Arg Val Leu
 225 230 235 240

Ser Glu Pro Asn Pro Arg Pro Val Phe Gly Ile Cys Leu Gly His Gln
 245 250 255

Leu Leu Ala Leu Ala Ile Gly Ala Lys Thr Tyr Lys Met Arg Tyr Gly
 260 265 270

Asn Arg Gly His Asn Gln Pro Cys Leu Leu Val Gly Ser Gly Arg Cys
 275 280 285

Phe Leu Thr Ser Gln Asn His Gly Phe Ala Val Glu Thr Asp Ser Leu
 290 295 300

Pro Ala Asp Trp Ala Pro Leu Phe Thr Asn Ala Asn Asp Gly Ser Asn
 305 310 315 320

Glu Gly Ile Val His Asn Ser Leu Pro Phe Phe Ser Val Gln Phe His
 325 330 335

Pro Glu His Gln Ala Gly Pro Ser Asp Met Glu Leu Leu Phe Asp Ile
 340 345 350

Phe Leu Glu Thr Val Lys Glu Ala Thr Ala Gly Asn Pro Gly Gly Gln
 355 360 365

Thr Val Arg Glu Arg Leu Thr Glu Arg Leu Cys Pro Pro Gly Ile Pro
 370 375 380

Thr Pro Gly Ser Gly Leu Pro Pro Pro Arg Lys Val Leu Ile Leu Gly
 385 390 395 400

Ser Gly Gly Leu Ser Ile Gly Gln Ala Gly Glu Phe Asp Tyr Ser Gly
 405 410 415

Ser Gln Ala Ile Lys Ala Leu Lys Glu Glu Asn Ile Gln Thr Leu Leu

201/383

420					425					430					
Ile	Asn	Pro	Asn	Ile	Ala	Thr	Val	Gln	Thr	Ser	Gln	Gly	Leu	Ala	Asp
	435						440					445			
Lys	Val	Tyr	Phe	Leu	Pro	Ile	Thr	Pro	His	Tyr	Val	Thr	Gln	Val	Ile
	450					455					460				
Arg	Asn	Glu	Arg	Pro	Asp	Gly	Val	Leu	Leu	Thr	Phe	Gly	Gly	Gln	Thr
465					470					475					480
Ala	Leu	Asn	Cys	Gly	Val	Glu	Leu	Thr	Lys	Ala	Gly	Val	Leu	Ala	Arg
				485					490					495	
Tyr	Gly	Val	Arg	Val	Leu	Gly	Thr	Thr	Val	Glu	Thr	Ile	Glu	Leu	Thr
			500					505					510		
Glu	Asp	Arg	Arg	Ala	Phe	Ala	Ala	Arg	Met	Ala	Glu	Ile	Gly	Glu	His
	515						520					525			
Val	Ala	Pro	Ser	Glu	Ala	Gly	Asn	Ser	Leu	Glu	Gln	Ala	Gln	Ala	Ala
	530					535					540				
Ala	Glu	Arg	Leu	Gly	Tyr	Pro	Val	Leu	Val	Arg	Ala	Ala	Phe	Ala	Val
545					550					555					560
Gly	Gly	Leu	Gly	Ser	Gly	Phe	Ala	Ser	Asn	Arg	Glu	Glu	Leu	Ser	Ala
				565					570					575	
Leu	Val	Ala	Pro	Ala	Phe	Ala	His	Thr	Ser	Gln	Val	Leu	Val	Asp	Lys
			580					585					590		
Ser	Leu	Lys	Gly	Trp	Lys	Glu	Ile	Glu	Tyr	Glu	Val	Val	Arg	Asp	Ala
	595						600					605			
Tyr	Gly	Asn	Cys	Val	Thr	Val	Cys	Asn	Met	Glu	Asn	Leu	Asp	Pro	Leu
	610					615					620				
Gly	Ile	His	Thr	Gly	Glu	Ser	Ile	Val	Val	Ala	Pro	Ser	Gln	Thr	Leu
625					630					635					640
Asn	Asp	Arg	Glu	Tyr	Gln	Leu	Leu	Arg	Gln	Thr	Ala	Ile	Lys	Val	Thr
			645						650					655	
Gln	His	Leu	Gly	Ile	Val	Gly	Glu	Cys	Asn	Val	Gln	Tyr	Ala	Leu	Asn
			660					665					670		

Pro Glu Ser Glu Gln Tyr Tyr Ile Ile Glu Val Asn Ala Arg Leu Ser
675 680 685

Arg Ser Ser Ala Leu Ala Ser Lys Ala Thr Gly Tyr Pro Leu Ala Tyr
690 695 700

Val Ala Ala Lys Leu Ala Leu Gly Ile Pro Leu Pro Glu Leu Arg Asn
705 710 715 720

Ser Val Thr Gly Gly Thr Ala Ala Phe Glu Pro Ser Val Asp Tyr Cys
725 730 735

Val Val Lys Ile Pro Arg Trp Asp Leu Ser Lys Phe Leu Arg Val Ser
740 745 750

Thr Lys Ile Gly Ser Cys Met Lys Ser Val Gly Glu Val Met Gly Ile
755 760 765

Gly Arg Ser Phe Glu Glu Ala Phe Gln Lys Ala Leu Arg Met Val Asp
770 775 780

Glu Asn Cys Val Gly Phe Asp His Thr Val Lys Pro Val Ser Asp Met
785 790 795 800

Glu Leu Glu Thr Pro Thr Asp Lys Arg Ile Phe Val Val Ala Ala Ala
805 810 815

Leu Trp Ala Gly Tyr Ser Val Asp Arg Leu Tyr Glu Leu Thr Arg Ile
820 825 830

Asp Arg Trp Phe Leu His Arg Met Lys Arg Ile Ile Ala His Ala Gln
835 840 845

Leu Leu Glu Gln His Arg Gly Gln Pro Leu Pro Pro Asp Leu Leu Gln
850 855 860

Gln Ala Lys Cys Leu Gly Phe Ser Asp Lys Gln Ile Ala Leu Ala Val
865 870 875 880

Leu Ser Thr Glu Leu Ala Val Arg Lys Leu Arg Gln Glu Leu Gly Ile
885 890 895

Cys Pro Ala Val Lys Gln Ile Asp Thr Val Ala Ala Glu Trp Pro Ala
900 905 910

Gln Thr Asn Tyr Leu Tyr Leu Thr Tyr Trp Gly Thr Thr His Asp Leu
915 920 925

Thr Phe Arg Thr Pro His Val Leu Val Leu Gly Ser Gly Val Tyr Arg
930 935 940

Ile Gly Ser Ser Val Glu Phe Asp Trp Cys Ala Val Gly Cys Ile Gln
945 950 955 960

Gln Leu Arg Lys Met Gly Tyr Lys Thr Ile Met Val Asn Tyr Asn Pro
965 970 975

Glu Thr Val Ser Thr Asp Tyr Asp Met Cys Asp Arg Leu Tyr Phe Asp
980 985 990

Glu Ile Ser Phe Glu Val Val Met Asp Ile Tyr Glu Leu Glu Asn Pro
995 1000 1005

Glu Gly Val Ile Leu Ser Met Gly Gly Gln Leu Pro Asn Asn Met
1010 1015 1020

Ala Met Ala Leu His Arg Gln Gln Cys Arg Val Leu Gly Thr Ser
1025 1030 1035

Pro Glu Ala Ile Asp Ser Ala Glu Asn Arg Phe Lys Phe Ser Arg
1040 1045 1050

Leu Leu Asp Thr Ile Gly Ile Ser Gln Pro Gln Trp Arg Glu Leu
1055 1060 1065

Ser Asp Leu Glu Ser Ala Arg Gln Phe Cys Gln Thr Val Gly Tyr
1070 1075 1080

Pro Cys Val Val Arg Pro Ser Tyr Val Leu Ser Gly Ala Ala Met
1085 1090 1095

Asn Val Ala Tyr Thr Asp Gly Asp Leu Glu Arg Phe Leu Ser Ser
1100 1105 1110

Ala Ala Ala Val Ser Lys Glu His Pro Val Val Ile Ser Lys Phe
1115 1120 1125

Ile Gln Glu Ala Lys Glu Ile Asp Val Asp Ala Val Ala Ser Asp
1130 1135 1140

Gly Val	Val Ala Ala Ile Ala	Ile Ser Glu His Val	Glu Asn Ala
1145	1150	1155	
Gly Val	His Ser Gly Asp Ala	Thr Leu Val Thr Pro	Pro Gln Asp
1160	1165	1170	
Ile Thr	Ala Lys Thr Leu Glu	Arg Ile Lys Ala Ile	Val His Ala
1175	1180	1185	
Val Gly	Gln Glu Leu Gln Val	Thr Gly Pro Phe Asn	Leu Gln Leu
1190	1195	1200	
Ile Ala	Lys Asp Asp Gln Leu	Lys Val Ile Glu Cys	Asn Val Arg
1205	1210	1215	
Val Ser	Arg Ser Phe Pro Phe	Val Ser Lys Thr Leu	Gly Val Asp
1220	1225	1230	
Leu Val	Ala Leu Ala Thr Arg	Val Ile Met Gly Glu	Glu Val Glu
1235	1240	1245	
Pro Val	Gly Leu Met Thr Gly	Ser Gly Val Val Gly	Val Lys Val
1250	1255	1260	
Pro Gln	Phe Ser Phe Ser Arg	Leu Ala Gly Ala Asp	Val Val Leu
1265	1270	1275	
Gly Val	Glu Met Thr Ser Thr	Gly Glu Val Ala Gly	Phe Gly Glu
1280	1285	1290	
Ser Arg	Cys Glu Ala Tyr Leu	Lys Ala Met Leu Ser	Thr Gly Phe
1295	1300	1305	
Lys Ile	Pro Lys Lys Asn Ile	Leu Leu Thr Ile Gly	Ser Tyr Lys
1310	1315	1320	
Asn Lys	Ser Glu Leu Leu Pro	Thr Val Arg Leu Leu	Glu Ser Leu
1325	1330	1335	
Gly Tyr	Ser Leu Tyr Ala Ser	Leu Gly Thr Ala Asp	Phe Tyr Thr
1340	1345	1350	
Glu His	Gly Val Lys Val Thr	Ala Val Asp Trp His	Phe Glu Glu
1355	1360	1365	
Ala Val	Asp Gly Glu Cys Pro	Pro Gln Arg Ser Ile	Leu Glu Gln

1370	1375	1380
Leu Ala Glu Lys Asn Phe Glu	Leu Val Ile Asn Leu	Ser Met Arg
1385	1390	1395
Gly Ala Gly Gly Arg Arg Leu	Ser Ser Phe Val Thr	Lys Gly Tyr
1400	1405	1410
Arg Thr Arg Arg Leu Ala Ala	Asp Phe Ser Val Pro	Leu Ile Ile
1415	1420	1425
Asp Ile Lys Cys Thr Lys Leu	Phe Val Glu Ala Leu	Gly Gln Ile
1430	1435	1440
Gly Pro Ala Pro Pro Leu Lys	Val His Val Asp Cys	Met Thr Ser
1445	1450	1455
Gln Lys Leu Val Arg Leu Pro	Gly Leu Ile Asp Val	His Val His
1460	1465	1470
Leu Arg Glu Pro Gly Gly Thr	His Lys Glu Asp Phe	Ala Ser Gly
1475	1480	1485
Thr Ala Ala Ala Leu Ala Gly	Gly Ile Thr Met Val	Cys Ala Met
1490	1495	1500
Pro Asn Thr Arg Pro Pro Ile	Ile Asp Ala Pro Ala	Leu Ala Leu
1505	1510	1515
Ala Gln Lys Leu Ala Glu Ala	Gly Ala Arg Cys Asp	Phe Ala Leu
1520	1525	1530
Phe Leu Gly Ala Ser Ser Glu	Asn Ala Gly Thr Leu	Gly Thr Val
1535	1540	1545
Ala Gly Ser Ala Ala Gly Leu	Lys Leu Tyr Leu Asn	Glu Thr Phe
1550	1555	1560
Ser Glu Leu Arg Leu Asp Ser	Val Val Gln Trp Met	Glu His Phe
1565	1570	1575
Glu Thr Trp Pro Ser His Leu	Pro Ile Val Ala His	Ala Glu Gln
1580	1585	1590
Gln Thr Val Ala Ala Val Leu	Met Val Ala Gln Leu	Thr Gln Arg
1595	1600	1605

Ser Val His Ile Cys His Val Ala Arg Lys Glu Glu Ile Leu Leu
1610 1615 1620

Ile Lys Ala Ala Lys Ala Arg Gly Leu Pro Val Thr Cys Glu Val
1625 1630 1635

Ala Pro His His Leu Phe Leu Ser His Asp Asp Leu Glu Arg Leu
1640 1645 1650

Gly Pro Gly Lys Gly Glu Val Arg Pro Glu Leu Gly Ser Arg Gln
1655 1660 1665

Asp Val Glu Ala Leu Trp Glu Asn Met Ala Val Ile Asp Cys Phe
1670 1675 1680

Ala Ser Asp His Ala Pro His Thr Leu Glu Glu Lys Cys Gly Ser
1685 1690 1695

Arg Pro Pro Pro Gly Phe Pro Gly Leu Glu Thr Met Leu Pro Leu
1700 1705 1710

Leu Leu Thr Ala Val Ser Glu Gly Arg Leu Ser Leu Asp Asp Leu
1715 1720 1725

Leu Gln Arg Leu His His Asn Pro Arg Arg Ile Phe His Leu Pro
1730 1735 1740

Pro Gln Glu Asp Thr Tyr Val Glu Val Asp Leu Glu His Glu Trp
1745 1750 1755

Thr Ile Pro Ser His Met Pro Phe Ser Lys Ala His Trp Thr Pro
1760 1765 1770

Phe Glu Gly Gln Lys Val Lys Gly Thr Val Arg Arg Val Val Leu
1775 1780 1785

Arg Gly Glu Val Ala Tyr Ile Asp Gly Gln Val Leu Val Pro Pro
1790 1795 1800

Gly Tyr Gly Gln Asp Val Arg Lys Trp Pro Gln Gly Ala Val Pro
1805 1810 1815

Gln Leu Pro Pro Ser Ala Pro Ala Thr Ser Glu Met Thr Thr Thr
1820 1825 1830

Pro Glu	Arg Pro Arg Arg Gly	Ile Pro Gly Leu Pro	Asp Gly Arg
1835		1840	1845
Phe His	Leu Pro Pro Arg Ile	His Arg Ala Ser Asp	Pro Gly Leu
1850		1855	1860
Pro Ala	Val Phe Leu Arg Pro	Gly Ala Gly Ile Pro	Arg Gly Ser
1865		1870	1875
Arg Ala	Trp Ala Glu Glu Pro	Lys Glu Lys Ser Ser	Arg Lys Val
1880		1885	1890
Ala Glu	Pro Glu Leu Met Gly	Thr Pro Asp Gly Thr	Cys Tyr Pro
1895		1900	1905
Pro Pro	Pro Val Pro Arg Gln	Ala Ser Pro Gln Asn	Leu Gly Thr
1910		1915	1920
Pro Gly	Leu Leu His Pro Gln	Thr Ser Pro Leu Leu	His Ser Leu
1925		1930	1935
Val Gly	Gln His Ile Leu Ser	Val Gln Gln Phe Thr	Lys Asp Gln
1940		1945	1950
Met Ser	His Leu Phe Asn Val	Ala His Thr Leu Arg	Met Met Val
1955		1960	1965
Gln Lys	Glu Arg Ser Leu Asp	Ile Leu Lys Gly Lys	Val Met Ala
1970		1975	1980
Ser Met	Phe Tyr Glu Val Ser	Thr Arg Thr Ser Ser	Ser Phe Ala
1985		1990	1995
Ala Ala	Met Ala Arg Leu Gly	Gly Ala Val Leu Ser	Phe Ser Glu
2000		2005	2010
Ala Thr	Ser Ser Val Gln Lys	Gly Glu Ser Leu Ala	Asp Ser Val
2015		2020	2025
Gln Thr	Met Ser Cys Tyr Ala	Asp Val Val Val Leu	Arg His Pro
2030		2035	2040
Gln Pro	Gly Ala Val Glu Leu	Ala Ala Lys His Cys	Arg Arg Pro
2045		2050	2055

208/383

Val Ile Asn Ala Gly Asp Gly Val Gly Glu His Pro Thr Gln Ala
2060 2065 2070

Leu Leu Asp Ile Phe Thr Ile Arg Glu Glu Leu Gly Thr Val Asn
2075 2080 2085

Gly Met Thr Ile Thr Met Val Gly Asp Leu Lys His Gly Arg Thr
2090 2095 2100

Val His Ser Leu Ala Cys Leu Leu Thr Gln Tyr Arg Val Ser Leu
2105 2110 2115

Arg Tyr Val Ala Pro Pro Ser Leu Arg Met Pro Pro Thr Val Arg
2120 2125 2130

Ala Phe Val Ala Ser Arg Gly Thr Lys Gln Glu Glu Phe Glu Ser
2135 2140 2145

Ile Glu Glu Ala Leu Pro Asp Thr Asp Val Leu Tyr Met Thr Arg
2150 2155 2160

Ile Gln Lys Glu Arg Phe Gly Ser Thr Gln Glu Tyr Glu Ala Cys
2165 2170 2175

Phe Gly Gln Phe Ile Leu Thr Pro His Ile Met Thr Arg Ala Lys
2180 2185 2190

Lys Lys Met Val Val Met His Pro Met Pro Arg Val Asn Glu Ile
2195 2200 2205

Ser Val Glu Val Asp Ser Asp Pro Arg Ala Ala Tyr Phe Arg Gln
2210 2215 2220

Ala Glu Asn Gly Met Tyr Ile Arg Met Ala Leu Leu Ala Thr Val
2225 2230 2235

Leu Gly Arg Phe
2240

<210> 130
<211> 371
<212> PRT
<213> Homo sapien

<400> 130

Met Tyr Ile Cys Pro Leu Val Leu Phe Ala Ala Glu Glu Pro Lys Glu
1 5 10 15

Lys Ser Ser Arg Lys Val Ala Glu Pro Glu Leu Met Gly Thr Pro Asp
20 25 30

Gly Thr Cys Tyr Pro Pro Pro Val Pro Arg Gln Ala Ser Pro Gln
35 40 45

Asn Leu Gly Thr Pro Gly Leu Leu His Pro Gln Thr Ser Pro Leu Leu
50 55 60

His Ser Leu Val Gly Gln His Ile Leu Ser Val Gln Gln Phe Thr Lys
65 70 75 80

Asp Gln Met Ser His Leu Phe Asn Val Ala His Thr Leu Arg Met Met
85 90 95

Val Gln Lys Glu Arg Ser Leu Asp Ile Leu Lys Gly Lys Val Met Ala
100 105 110

Ser Met Phe Tyr Glu Val Ser Thr Arg Thr Ser Ser Ser Phe Ala Ala
115 120 125

Ala Met Ala Arg Leu Gly Gly Ala Val Leu Ser Phe Ser Glu Ala Thr
130 135 140

Ser Ser Val Gln Lys Gly Glu Ser Leu Ala Asp Ser Val Gln Thr Met
145 150 155 160

Ser Cys Tyr Ala Asp Val Val Val Leu Arg His Pro Gln Pro Gly Ala
165 170 175

Val Glu Leu Ala Ala Lys His Cys Arg Arg Pro Val Ile Asn Ala Gly
180 185 190

Asp Gly Val Gly Glu His Pro Thr Gln Ala Leu Leu Asp Ile Phe Thr
195 200 205

Ile Arg Glu Glu Leu Gly Thr Val Asn Gly Met Thr Ile Thr Met Val
210 215 220

Gly Asp Leu Lys His Gly Arg Thr Val His Ser Leu Ala Cys Leu Leu
225 230 235 240

Thr Gln Tyr Arg Val Ser Leu Arg Tyr Val Ala Pro Pro Ser Leu Arg
245 250 255

Met Pro Pro Thr Val Arg Ala Phe Val Ala Ser Arg Gly Thr Lys Gln
260 265 270

Glu Glu Phe Glu Ser Ile Glu Glu Ala Leu Pro Asp Thr Asp Val Leu
275 280 285

Tyr Met Thr Arg Ile Gln Lys Glu Arg Phe Gly Ser Thr Gln Glu Tyr
290 295 300

Glu Ala Cys Phe Gly Gln Phe Ile Leu Thr Pro His Ile Met Thr Arg
305 310 315 320

Ala Lys Lys Lys Met Val Val Met His Pro Met Pro Arg Val Asn Glu
325 330 335

Ile Ser Val Glu Val Asp Ser Asp Pro Arg Ala Ala Tyr Phe Arg Gln
340 345 350

Ala Glu Asn Gly Met Tyr Ile Arg Met Ala Leu Leu Ala Thr Val Leu
355 360 365

Gly Arg Phe
370

<210> 131
<211> 970
<212> PRT
<213> Homo sapien

<400> 131

Met Ala Gly Ala Leu Ala Gly Leu Ala Ala Gly Leu Gln Val Pro Arg
1 5 10 15

Val Ala Pro Ser Pro Asp Ser Asp Ser Asp Thr Asp Ser Glu Asp Pro
20 25 30

Ser Leu Arg Arg Ser Ala Gly Gly Leu Leu Arg Ser Gln Val Ile His
35 40 45

Ser Gly His Phe Met Val Ser Ser Pro His Ser Asp Ser Leu Pro Arg
50 55 60

Arg Arg Asp Gln Glu Gly Ser Val Gly Pro Ser Asp Phe Gly Pro Arg
65 70 75 80

Ser Ile Asp Pro Thr Leu Thr Arg Leu Phe Glu Cys Leu Ser Leu Ala

Leu Phe Thr Met Thr Gln Ser Gly Pro Ser Pro Leu Gln Leu Pro Pro
325 330 335

Glu Asp Ala Tyr Val Gly Asn Ala Asp Met Ile Gln Pro Asp Leu Thr
340 345 350

Pro Leu Gln Pro Ser Leu Asp Asp Phe Met Asp Ile Ser Asp Phe Phe
355 360 365

Thr Asn Ser Arg Leu Pro Gln Pro Pro Met Pro Ser Asn Phe Pro Glu
370 375 380

Pro Pro Ser Phe Ser Pro Val Val Asp Ser Leu Phe Ser Ser Gly Thr
385 390 395 400

Leu Gly Pro Glu Val Pro Pro Ala Ser Ser Ala Met Thr His Leu Ser
405 410 415

Gly His Ser Arg Leu Gln Ala Arg Asn Ser Cys Pro Gly Pro Leu Asp
420 425 430

Ser Ser Ala Phe Leu Ser Ser Asp Phe Leu Leu Pro Glu Asp Pro Lys
435 440 445

Pro Arg Leu Pro Pro Pro Pro Val Pro Pro Pro Leu Leu His Tyr Pro
450 455 460

Pro Pro Ala Lys Val Pro Gly Leu Glu Pro Cys Pro Pro Pro Pro Phe
465 470 475 480

Pro Pro Met Ala Pro Pro Thr Ala Leu Leu Gln Glu Glu Pro Leu Phe
485 490 495

Ser Pro Arg Phe Pro Phe Pro Thr Val Pro Pro Ala Pro Gly Val Ser
500 505 510

Pro Leu Pro Ala Pro Ala Ala Phe Pro Pro Thr Pro Gln Ser Val Pro
515 520 525

Ser Pro Ala Pro Thr Pro Phe Pro Ile Glu Leu Leu Pro Leu Gly Tyr
530 535 540

Ser Glu Pro Ala Phe Gly Pro Cys Phe Ser Met Pro Arg Gly Lys Pro
545 550 555 560

Pro Ala Pro Ser Pro Arg Gly Gln Lys Ala Ser Pro Pro Thr Leu Ala
565 570 575

Pro Ala Thr Ala Ser Pro Pro Thr Thr Ala Gly Ser Asn Asn Pro Cys
 580 585 590

Leu Thr Gln Leu Leu Thr Ala Ala Lys Pro Glu Gln Ala Leu Glu Pro
 595 600 605

Pro Leu Val Ser Ser Thr Leu Leu Arg Ser Pro Gly Ser Pro Gln Glu
 610 615 620

Thr Val Pro Glu Phe Pro Cys Thr Phe Leu Pro Pro Thr Pro Ala Pro
 625 630 635 640

Thr Pro Pro Arg Pro Pro Pro Gly Pro Ala Thr Leu Ala Pro Ser Arg
 645 650 655

Pro Leu Leu Val Pro Lys Ala Glu Arg Leu Ser Pro Pro Ala Pro Ser
 660 665 670

Gly Lys Glu Arg Gly Cys Arg Asp Trp Gly Asn Leu Gly Asp Glu Gly
 675 680 685

Lys Arg Arg Lys Lys Lys Gly Thr Gly Ser Gly Ala Arg Trp Glu Glu
 690 695 700

Gly Gly Asn Gly Asp Pro Phe Pro Trp Val Gly Leu Ser Val Gly Leu
 705 710 715 720

Ser Val Pro Thr Thr Gly Ser Glu Arg Arg Leu Ser Gly Asp Leu Ser
 725 730 735

Ser Met Pro Gly Pro Gly Thr Leu Ser Val Arg Val Ser Pro Pro Gln
 740 745 750

Pro Ile Leu Ser Arg Gly Arg Pro Asp Ser Asn Lys Thr Glu Asn Arg
 755 760 765

Arg Ile Thr His Ile Ser Ala Glu Gln Lys Arg Arg Phe Asn Ile Lys
 770 775 780

Leu Gly Phe Asp Thr Leu His Gly Leu Val Ser Thr Leu Ser Ala Gln
 785 790 795 800

Pro Ser Leu Lys Val Ser Lys Ala Thr Thr Leu Gln Lys Thr Ala Glu
 805 810 815

214/383

Tyr Ile Leu Met Leu Gln Gln Glu Arg Ala Gly Leu Gln Glu Glu Ala
 820 825 830

Gln Gln Leu Arg Asp Glu Ile Glu Glu Leu Asn Ala Ala Ile Asn Leu
 835 840 845

Cys Gln Gln Gln Leu Pro Ala Thr Gly Val Pro Ile Thr His Gln Arg
 850 855 860

Phe Asp Gln Met Arg Asp Met Phe Asp Asp Tyr Val Arg Thr Arg Thr
 865 870 875 880

Leu His Asn Trp Lys Phe Trp Val Phe Ser Ile Leu Ile Arg Pro Leu
 885 890 895

Phe Glu Ser Phe Asn Gly Met Val Ser Thr Ala Ser Val His Thr Leu
 900 905 910

Arg Gln Thr Ser Leu Ala Trp Leu Asp Gln Tyr Cys Ser Leu Pro Ala
 915 920 925

Leu Arg Pro Thr Val Leu Asn Ser Leu Arg Gln Leu Gly Thr Ser Thr
 930 935 940

Ser Ile Leu Thr Asp Pro Gly Arg Ile Pro Glu Gln Ala Thr Arg Ala
 945 950 955 960

Val Thr Glu Gly Thr Leu Gly Lys Pro Leu
 965 970

<210> 132
 <211> 719
 <212> PRT
 <213> Homo sapien

<400> 132

Ala Val Pro Arg Ala Ala Arg Ser Arg Asp Gln Ala Val Ala Ala Ala
 1 5 10 15

Thr Ala Met Ala Gly Ala Leu Ala Gly Leu Ala Ala Gly Leu Gln Val
 20 25 30

Pro Arg Val Ala Pro Ser Pro Asp Ser Asp Ser Asp Thr Asp Ser Glu
 35 40 45

Asp Pro Ser Leu Arg Arg Ser Ala Gly Gly Leu Leu Arg Ser Gln Val
 50 55 60

Ile His Ser Gly His Phe Met Val Ser Ser Pro His Ser Asp Ser Leu
65 70 75 80

Pro Arg Arg Arg Asp Gln Glu Gly Ser Val Gly Pro Ser Asp Phe Gly
85 90 95

Pro Arg Ser Ile Asp Pro Thr Leu Thr Arg Leu Phe Glu Cys Leu Ser
100 105 110

Leu Ala Tyr Ser Gly Lys Leu Val Ser Pro Lys Trp Lys Asn Phe Lys
115 120 125

Gly Leu Lys Leu Leu Cys Arg Asp Lys Ile Arg Leu Asn Asn Ala Ile
130 135 140

Trp Arg Ala Trp Tyr Ile Gln Tyr Val Lys Arg Arg Lys Ser Pro Val
145 150 155 160

Cys Gly Phe Val Thr Pro Leu Gln Gly Pro Glu Ala Asp Ala His Arg
165 170 175

Lys Pro Glu Ala Val Val Leu Glu Gly Asn Tyr Trp Lys Arg Arg Ile
180 185 190

Glu Val Val Met Arg Glu Tyr His Lys Trp Arg Ile Tyr Tyr Lys Lys
195 200 205

Arg Val Ser Gly Gly Gly Pro Gly Arg Pro Gln Ser Phe Pro Pro Ala
210 215 220

Ala Ala Gly Tyr Arg Pro Pro Arg Lys Ile Pro Gly Lys Gly Ile Leu
225 230 235 240

Thr Pro Glu Leu Ala Pro Leu Gly Pro Ser Ile Gln Ser Arg Ala Asp
245 250 255

Ser Ala Thr Val Trp Pro Gln Arg Leu Leu Ala Ala Ser Leu Pro Arg
260 265 270

Gly Arg Leu Arg Lys Pro Ser Arg Glu Asp Asp Leu Leu Ala Pro Lys
275 280 285

Gln Ala Glu Gly Arg Trp Pro Pro Pro Glu Gln Trp Cys Lys Gln Leu
290 295 300

Phe Ser Ser Val Val Pro Val Leu Leu Gly Asp Pro Glu Glu Glu Pro
 305 310 315 320

Gly Gly Arg Gln Leu Leu Asp Leu Asn Cys Phe Leu Ser Asp Ile Ser
 325 330 335

Asp Thr Leu Phe Thr Met Thr Gln Ser Gly Pro Ser Pro Leu Gln Leu
 340 345 350

Pro Pro Glu Asp Ala Tyr Val Gly Asn Ala Asp Met Ile Gln Pro Asp
 355 360 365

Leu Thr Pro Leu Gln Pro Ser Leu Asp Asp Phe Met Asp Ile Ser Asp
 370 375 380

Phe Phe Thr Asn Ser Arg Leu Pro Gln Pro Pro Met Pro Ser Asn Phe
 385 390 395 400

Pro Glu Pro Pro Ser Phe Ser Pro Val Val Asp Ser Leu Phe Ser Ser
 405 410 415

Gly Thr Leu Gly Pro Glu Val Pro Pro Ala Ser Ser Ala Met Thr His
 420 425 430

Leu Ser Gly His Ser Arg Leu Gln Ala Arg Asn Ser Cys Pro Gly Pro
 435 440 445

Leu Asp Ser Ser Ala Phe Leu Ser Ser Asp Phe Leu Leu Pro Glu Asp
 450 455 460

Pro Lys Pro Arg Leu Pro Pro Pro Pro Val Pro Pro Pro Leu Leu His
 465 470 475 480

Tyr Pro Pro Pro Ala Lys Val Pro Gly Leu Glu Pro Cys Pro Pro Pro
 485 490 495

Pro Phe Pro Pro Met Ala Pro Pro Thr Ala Leu Leu Gln Glu Glu Pro
 500 505 510

Leu Phe Ser Pro Arg Phe Pro Phe Pro Thr Val Pro Pro Ala Pro Gly
 515 520 525

Val Ser Pro Leu Pro Ala Pro Ala Ala Phe Pro Pro Thr Pro Gln Ser
 530 535 540

Val Pro Ser Pro Ala Pro Thr Pro Phe Pro Ile Glu Leu Leu Pro Leu
545 550 555 560

Gly Tyr Ser Glu Pro Ala Phe Gly Pro Cys Phe Ser Met Pro Arg Gly
565 570 575

Lys Pro Pro Ala Pro Ser Pro Arg Gly Gln Lys Ala Ser Pro Pro Thr
580 585 590

Leu Ala Pro Ala Thr Ala Ser Pro Pro Thr Thr Ala Gly Ser Asn Asn
595 600 605

Pro Cys Leu Thr Gln Leu Leu Thr Ala Ala Lys Pro Glu Gln Ala Leu
610 615 620

Glu Pro Pro Leu Val Ser Ser Thr Leu Leu Arg Ser Pro Gly Ser Pro
625 630 635 640

Gln Glu Thr Val Pro Glu Phe Pro Cys Thr Phe Leu Pro Pro Thr Pro
645 650 655

Ala Pro Thr Pro Pro Arg Pro Pro Pro Gly Pro Ala Thr Leu Ala Pro
660 665 670

Ser Arg Pro Leu Leu Val Pro Lys Ala Glu Arg Leu Ser Pro Pro Ala
675 680 685

Pro Ser Gly Lys Glu Arg Gly Cys Arg Asp Trp Gly Asn Leu Gly Asp
690 695 700

Glu Gly Lys Arg Arg Lys Lys Lys Gly Thr Gly Ser Gly Ala Arg
705 710 715

<210> 133
<211> 629
<212> PRT
<213> Homo sapien

<400> 133

Met Ala Val Pro Trp Glu Gln Ala Ser Leu Gly Gly Gln Arg Pro Cys
1 5 10 15

Leu Gly Thr Gln Arg Pro Ala Thr Asp Phe Phe Thr Asn Ser Arg Leu
20 25 30

Pro Gln Pro Pro Met Pro Ser Asn Phe Pro Glu Pro Pro Ser Phe Ser
35 40 45

Pro Val Val Asp Ser Leu Phe Ser Ser Gly Thr Leu Gly Pro Glu Val
50 55 60

Pro Pro Ala Ser Ser Ala Met Thr His Leu Ser Gly His Ser Arg Leu
65 70 75 80

Gln Ala Arg Asn Ser Cys Pro Gly Pro Leu Asp Ser Ser Ala Phe Leu
85 90 95

Ser Ser Asp Phe Leu Leu Pro Glu Asp Pro Lys Pro Arg Leu Pro Pro
100 105 110

Pro Pro Val Pro Pro Pro Leu Leu His Tyr Pro Pro Pro Ala Lys Val
115 120 125

Pro Gly Leu Glu Pro Cys Pro Pro Pro Phe Pro Pro Met Ala Pro
130 135 140

Pro Thr Ala Leu Leu Gln Glu Glu Pro Leu Phe Ser Pro Arg Phe Pro
145 150 155 160

Phe Pro Thr Val Pro Pro Ala Pro Gly Val Ser Pro Leu Pro Ala Pro
165 170 175

Ala Ala Phe Pro Pro Thr Pro Gln Ser Val Pro Ser Pro Ala Pro Thr
180 185 190

Pro Phe Pro Ile Glu Leu Leu Pro Leu Gly Tyr Ser Glu Pro Ala Phe
195 200 205

Gly Pro Cys Phe Ser Met Pro Arg Gly Lys Pro Pro Ala Pro Ser Pro
210 215 220

Arg Gly Gln Lys Ala Ser Pro Pro Thr Leu Ala Pro Ala Thr Ala Ser
225 230 235 240

Pro Pro Thr Thr Ala Gly Ser Asn Asn Pro Cys Leu Thr Gln Leu Leu
245 250 255

Thr Ala Ala Lys Pro Glu Gln Ala Leu Glu Pro Pro Leu Val Ser Ser
260 265 270

Thr Leu Leu Arg Ser Pro Gly Ser Pro Gln Glu Thr Val Pro Glu Phe
275 280 285

Pro Cys Thr Phe Leu Pro Pro Thr Pro Ala Pro Thr Pro Pro Arg Pro
290 295 300

Pro Pro Gly Pro Ala Thr Leu Ala Pro Ser Arg Pro Leu Leu Val Pro
305 310 315 320

Lys Ala Glu Arg Leu Ser Pro Pro Ala Pro Ser Gly Lys Glu Arg Gly
325 330 335

Cys Arg Asp Trp Gly Asn Leu Gly Asp Glu Gly Lys Arg Arg Lys Lys
340 345 350

Lys Gly Thr Gly Ser Gly Ala Arg Gly Glu Glu Gly Gly Asn Gly Asp
355 360 365

Pro Phe Pro Trp Val Gly Leu Ser Val Gly Leu Ser Val Pro Thr Thr
370 375 380

Gly Ser Glu Arg Arg Leu Ser Gly Asp Leu Ser Ser Met Pro Gly Pro
385 390 395 400

Gly Thr Leu Ser Val Arg Val Ser Pro Pro Gln Pro Ile Leu Ser Arg
405 410 415

Gly Arg Pro Asp Ser Asn Lys Thr Glu Asn Arg Arg Ile Thr His Ile
420 425 430

Ser Ala Glu Gln Lys Arg Arg Phe Asn Ile Lys Leu Gly Phe Asp Thr
435 440 445

Leu His Gly Leu Val Ser Thr Leu Ser Ala Gln Pro Ser Leu Lys Val
450 455 460

Ser Lys Ala Thr Thr Leu Gln Lys Thr Ala Glu Tyr Ile Leu Met Leu
465 470 475 480

Gln Gln Glu Arg Ala Gly Leu Gln Glu Glu Ala Gln Gln Leu Arg Asp
485 490 495

Glu Ile Glu Glu Leu Asn Ala Ala Ile Asn Leu Cys Gln Gln Gln Leu
500 505 510

Pro Ala Thr Gly Val Pro Ile Thr His Gln Arg Phe Asp Gln Met Arg
515 520 525

220/383

Asp Met Phe Asp Asp Tyr Val Arg Thr Arg Thr Leu His Asn Trp Lys
 530 535 540

Phe Trp Val Phe Ser Ile Leu Ile Arg Pro Leu Phe Glu Ser Phe Asn
 545 550 555 560

Gly Met Val Ser Thr Ala Ser Val His Thr Leu Arg Gln Thr Ser Leu
 565 570 575

Ala Trp Leu Asp Gln Tyr Cys Ser Leu Pro Ala Leu Arg Pro Thr Val
 580 585 590

Leu Asn Ser Leu Arg Gln Leu Gly Thr Ser Thr Ser Ile Leu Thr Asp
 595 600 605

Pro Gly Arg Ile Pro Glu Gln Ala Thr Arg Ala Val Thr Glu Gly Thr
 610 615 620

Leu Gly Lys Pro Leu
 625

<210> 134
 <211> 382
 <212> PRT
 <213> Homo sapien

<400> 134

Gly Thr Thr Pro Thr Pro Val Pro Val Pro Gly Gly Gly Gly Cys
 1 5 10 15

Pro Gly Ala Glu Val Cys Met Ala Val Pro Trp Glu Gln Ala Ser Leu
 20 25 30

Gly Gly Gln Arg Pro Cys Leu Gly Thr Gln Arg Pro Ala Thr Asp Phe
 35 40 45

Phe Thr Asn Ser Arg Leu Pro Gln Pro Pro Met Pro Ser Asn Phe Pro
 50 55 60

Glu Pro Pro Ser Phe Ser Pro Val Val Asp Ser Leu Phe Ser Ser Gly
 65 70 75 80

Thr Leu Gly Pro Glu Val Pro Pro Ala Ser Ser Ala Met Thr His Leu
 85 90 95

Ser Gly His Ser Arg Leu Gln Ala Arg Asn Ser Cys Pro Gly Pro Leu
 100 105 110

Asp Ser Ser Ala Phe Leu Ser Ser Asp Phe Leu Leu Pro Glu Asp Pro
 115 120 125

Lys Pro Arg Leu Pro Pro Pro Pro Val Pro Pro Pro Leu Leu His Tyr
 130 135 140

Pro Pro Pro Ala Lys Val Pro Gly Leu Glu Pro Cys Pro Pro Pro Pro
 145 150 155 160

Phe Pro Pro Met Ala Pro Pro Thr Ala Leu Leu Gln Glu Glu Pro Leu
 165 170 175

Phe Ser Pro Arg Phe Pro Phe Pro Thr Val Pro Pro Ala Pro Gly Val
 180 185 190

Ser Pro Leu Pro Ala Pro Ala Ala Phe Pro Pro Thr Pro Gln Ser Val
 195 200 205

Pro Ser Pro Ala Pro Thr Pro Phe Pro Ile Glu Leu Leu Pro Leu Gly
 210 215 220

Tyr Ser Glu Pro Ala Phe Gly Pro Cys Phe Ser Met Pro Arg Gly Lys
 225 230 235 240

Pro Pro Ala Pro Ser Pro Arg Gly Gln Lys Ala Ser Pro Pro Thr Leu
 245 250 255

Ala Pro Ala Thr Ala Ser Pro Pro Thr Thr Ala Gly Ser Asn Asn Pro
 260 265 270

Cys Leu Thr Gln Leu Leu Thr Ala Ala Lys Pro Glu Gln Ala Leu Glu
 275 280 285

Pro Pro Leu Val Ser Ser Thr Leu Leu Arg Ser Pro Gly Ser Pro Gln
 290 295 300

Glu Thr Val Pro Glu Phe Pro Cys Thr Phe Leu Pro Pro Thr Pro Ala
 305 310 315 320

Pro Thr Pro Pro Arg Pro Pro Pro Gly Pro Ala Thr Leu Ala Pro Ser
 325 330 335

Arg Pro Leu Leu Val Pro Lys Ala Glu Arg Leu Ser Pro Pro Ala Pro
 340 345 350

Ser Gly Lys Glu Arg Gly Cys Arg Asp Trp Gly Asn Leu Gly Asp Glu
 355 360 365

Gly Lys Arg Arg Lys Lys Lys Gly Thr Gly Ser Gly Ala Arg
 370 375 380

<210> 135
 <211> 1009
 <212> PRT
 <213> Homo sapien

<400> 135

Met Ala Gly Ala Leu Ala Gly Leu Ala Ala Gly Leu Gln Val Pro Arg
 1 5 10 15

Val Ala Pro Ser Pro Asp Ser Asp Ser Asp Thr Asp Ser Glu Asp Pro
 20 25 30

Ser Leu Arg Arg Ser Ala Gly Gly Leu Leu Arg Ser Gln Val Ile His
 35 40 45

Ser Gly His Phe Met Val Ser Ser Pro His Ser Asp Ser Leu Pro Arg
 50 55 60

Arg Arg Asp Gln Glu Gly Ser Val Gly Pro Ser Asp Phe Gly Pro Arg
 65 70 75 80

Ser Ile Asp Pro Thr Leu Thr Arg Leu Phe Glu Cys Leu Ser Leu Ala
 85 90 95

Tyr Ser Gly Lys Leu Val Ser Pro Lys Trp Lys Asn Phe Lys Gly Leu
 100 105 110

Lys Leu Leu Cys Arg Asp Lys Ile Arg Leu Asn Asn Ala Ile Trp Arg
 115 120 125

Ala Trp Tyr Ile Gln Tyr Val Lys Arg Arg Lys Ser Pro Val Cys Gly
 130 135 140

Phe Val Thr Pro Leu Gln Gly Pro Glu Ala Asp Ala His Arg Lys Pro
 145 150 155 160

Glu Ala Val Val Leu Glu Gly Asn Tyr Trp Lys Arg Arg Ile Glu Val
 165 170 175

Val Met Arg Glu Tyr His Lys Trp Arg Ile Tyr Tyr Lys Lys Arg Val

180	185	190
Ser Gly Gly Gly Pro Gly Arg Pro Gln Ser Phe Pro Pro Ala Ala Ala 195 200 205		
Gly Tyr Arg Pro Pro Arg Lys Ile Pro Gly Lys Gly Ile Leu Thr Pro 210 215 220		
Glu Leu Ala Pro Leu Gly Pro Ser Ile Gln Ser Arg Ala Asp Ser Ala 225 230 235 240		
Thr Val Trp Pro Gln Arg Leu Leu Ala Ala Ser Leu Pro Arg Gly Arg 245 250 255		
Val Ser Ser Cys Gly Lys Trp Gly Ile Ser Ser Leu Val Ser Arg Gly 260 265 270		
Asp Phe Gly Gly Lys Val Met Glu Asp Gly Ala Lys Gly Ser Gly Val 275 280 285		
Gln Leu Cys Val Ser Leu Gln Leu Arg Lys Pro Ser Arg Glu Asp Asp 290 295 300		
Leu Leu Ala Pro Lys Gln Ala Glu Gly Arg Trp Pro Pro Pro Glu Gln 305 310 315 320		
Trp Cys Lys Gln Leu Phe Ser Ser Val Val Pro Val Leu Leu Gly Asp 325 330 335		
Pro Glu Glu Glu Pro Gly Gly Arg Gln Leu Leu Asp Leu Asn Cys Phe 340 345 350		
Leu Ser Asp Ile Ser Asp Thr Leu Phe Thr Met Thr Gln Ser Gly Pro 355 360 365		
Ser Pro Leu Gln Leu Pro Pro Glu Asp Ala Tyr Val Gly Asn Ala Asp 370 375 380		
Met Ile Gln Pro Asp Leu Thr Pro Leu Gln Pro Ser Leu Asp Asp Phe 385 390 395 400		
Met Asp Ile Ser Asp Phe Phe Thr Asn Ser Arg Leu Pro Gln Pro Pro 405 410 415		
Met Pro Ser Asn Phe Pro Glu Pro Pro Ser Phe Ser Pro Val Val Asp 420 425 430		

Ser Leu Phe Ser Ser Gly Thr Leu Gly Pro Glu Val Pro Pro Ala Ser
435 440 445

Ser Ala Met Thr His Leu Ser Gly His Ser Arg Leu Gln Ala Arg Asn
450 455 460

Ser Cys Pro Gly Pro Leu Asp Ser Ser Ala Phe Leu Ser Ser Asp Phe
465 470 475 480

Leu Leu Pro Glu Asp Pro Lys Pro Arg Leu Pro Pro Pro Pro Val Pro
485 490 495

Pro Pro Leu Leu His Tyr Pro Pro Pro Ala Lys Val Pro Gly Leu Glu
500 505 510

Pro Cys Pro Pro Pro Pro Phe Pro Pro Met Ala Pro Pro Thr Ala Leu
515 520 525

Leu Gln Glu Glu Pro Leu Phe Ser Pro Arg Phe Pro Phe Pro Thr Val
530 535 540

Pro Pro Ala Pro Gly Val Ser Pro Leu Pro Ala Pro Ala Ala Phe Pro
545 550 555 560

Pro Thr Pro Gln Ser Val Pro Ser Pro Ala Pro Thr Pro Phe Pro Ile
565 570 575

Glu Leu Leu Pro Leu Gly Tyr Ser Glu Pro Ala Phe Gly Pro Cys Phe
580 585 590

Ser Met Pro Arg Gly Lys Pro Pro Ala Pro Ser Pro Arg Gly Gln Lys
595 600 605

Ala Ser Pro Pro Thr Leu Ala Pro Ala Thr Ala Ser Pro Pro Thr Thr
610 615 620

Ala Gly Ser Asn Asn Pro Cys Leu Thr Gln Leu Leu Thr Ala Ala Lys
625 630 635 640

Pro Glu Gln Ala Leu Glu Pro Pro Leu Val Ser Ser Thr Leu Leu Arg
645 650 655

Ser Pro Gly Ser Pro Gln Glu Thr Val Pro Glu Phe Pro Cys Thr Phe
660 665 670

Leu Pro Pro Thr Pro Ala Pro Thr Pro Pro Arg Pro Pro Pro Gly Pro
675 680 685

Ala Thr Leu Ala Pro Ser Arg Pro Leu Leu Val Pro Lys Ala Glu Arg
690 695 700

Leu Ser Pro Pro Ala Pro Ser Gly Lys Glu Arg Gly Cys Arg Asp Trp
705 710 715 720

Gly Asn Leu Gly Asp Glu Gly Lys Arg Arg Lys Lys Lys Gly Thr Gly
725 730 735

Ser Gly Ala Arg Trp Glu Glu Gly Gly Asn Gly Asp Pro Phe Pro Trp
740 745 750

Val Gly Leu Ser Val Gly Leu Ser Val Pro Thr Thr Gly Ser Glu Arg
755 760 765

Arg Leu Ser Gly Asp Leu Ser Ser Met Pro Gly Pro Gly Thr Leu Ser
770 775 780

Val Arg Val Ser Pro Pro Gln Pro Ile Leu Ser Arg Gly Arg Pro Asp
785 790 795 800

Ser Asn Lys Thr Glu Asn Arg Arg Ile Thr His Ile Ser Ala Glu Gln
805 810 815

Lys Arg Arg Phe Asn Ile Lys Leu Gly Phe Asp Thr Leu His Gly Leu
820 825 830

Val Ser Thr Leu Ser Ala Gln Pro Ser Leu Lys Val Ser Lys Ala Thr
835 840 845

Thr Leu Gln Lys Thr Ala Glu Tyr Ile Leu Met Leu Gln Gln Glu Arg
850 855 860

Ala Gly Leu Gln Glu Glu Ala Gln Gln Leu Arg Asp Glu Ile Glu Glu
865 870 875 880

Leu Asn Ala Ala Ile Asn Leu Cys Gln Gln Gln Leu Pro Ala Thr Gly
885 890 895

Val Pro Ile Thr His Gln Arg Phe Asp Gln Met Arg Asp Met Phe Asp
900 905 910

226/383

Asp Tyr Val Arg Thr Arg Thr Leu His Asn Trp Lys Phe Trp Val Phe
 915 920 925

Ser Ile Leu Ile Arg Pro Leu Phe Glu Ser Phe Asn Gly Met Val Ser
 930 935 940

Thr Ala Ser Val His Thr Leu Arg Gln Thr Ser Leu Ala Trp Leu Asp
 945 950 955 960

Gln Tyr Cys Ser Leu Pro Ala Leu Arg Pro Thr Val Leu Asn Ser Leu
 965 970 975

Arg Gln Leu Gly Thr Ser Thr Ser Ile Leu Thr Asp Pro Gly Arg Ile
 980 985 990

Pro Glu Gln Ala Thr Arg Ala Val Thr Glu Gly Thr Leu Gly Lys Pro
 995 1000 1005

Leu

<210> 136
 <211> 469
 <212> PRT
 <213> Homo sapien

<400> 136

Arg Arg Leu Trp Gly Glu Ser Asp Gly Gly Trp Gly Lys Gly Ser Gly
 1 5 10 15

Val Gln Leu Cys Val Ser Leu Gln Leu Arg Lys Pro Ser Arg Glu Asp
 20 25 30

Asp Leu Leu Ala Pro Lys Gln Ala Glu Gly Arg Trp Pro Pro Pro Glu
 35 40 45

Gln Trp Cys Lys Gln Leu Phe Ser Ser Val Val Pro Val Leu Leu Gly
 50 55 60

Asp Pro Glu Glu Glu Pro Gly Gly Arg Gln Leu Leu Asp Leu Asn Cys
 65 70 75 80

Phe Leu Ser Asp Ile Ser Asp Thr Leu Phe Thr Met Thr Gln Ser Gly
 85 90 95

Pro Ser Pro Leu Gln Leu Pro Pro Glu Asp Ala Tyr Val Gly Asn Ala
 100 105 110

Asp Met Ile Gln Pro Asp Leu Thr Pro Leu Gln Pro Ser Leu Asp Asp
 115 120 125

Phe Met Asp Ile Ser Asp Phe Phe Thr Asn Ser Arg Leu Pro Gln Pro
 130 135 140

Pro Met Pro Ser Asn Phe Pro Glu Pro Pro Ser Phe Ser Pro Val Val
 145 150 155 160

Asp Ser Leu Phe Ser Ser Gly Thr Leu Gly Pro Glu Val Pro Pro Ala
 165 170 175

Ser Ser Ala Met Thr His Leu Ser Gly His Ser Arg Leu Gln Ala Arg
 180 185 190

Asn Ser Cys Pro Gly Pro Leu Asp Ser Ser Ala Phe Leu Ser Ser Asp
 195 200 205

Phe Leu Leu Pro Glu Asp Pro Lys Pro Arg Leu Pro Pro Pro Pro Val
 210 215 220

Pro Pro Pro Leu Leu His Tyr Pro Pro Pro Ala Lys Val Pro Gly Leu
 225 230 235 240

Glu Pro Cys Pro Pro Pro Pro Phe Pro Pro Met Ala Pro Pro Thr Ala
 245 250 255

Leu Leu Gln Glu Glu Pro Leu Phe Ser Pro Arg Phe Pro Phe Pro Thr
 260 265 270

Val Pro Pro Ala Pro Gly Val Ser Pro Leu Pro Ala Pro Ala Ala Phe
 275 280 285

Pro Pro Thr Pro Gln Ser Val Pro Ser Pro Ala Pro Thr Pro Phe Pro
 290 295 300

Ile Glu Leu Leu Pro Leu Gly Tyr Ser Glu Pro Ala Phe Gly Pro Cys
 305 310 315 320

Phe Ser Met Pro Arg Gly Lys Pro Pro Ala Pro Ser Pro Arg Gly Gln
 325 330 335

Lys Ala Ser Pro Pro Thr Leu Ala Pro Ala Thr Ala Ser Pro Pro Thr
 340 345 350

Thr Ala Gly Ser Asn Asn Pro Cys Leu Thr Gln Leu Leu Thr Ala Ala
 355 360 365

Lys Pro Glu Gln Ala Leu Glu Pro Pro Leu Val Ser Ser Thr Leu Leu
 370 375 380

Arg Ser Pro Gly Ser Pro Gln Glu Thr Val Pro Glu Phe Pro Cys Thr
 385 390 395 400

Phe Leu Pro Pro Thr Pro Ala Pro Thr Pro Pro Arg Pro Pro Pro Gly
 405 410 415

Pro Ala Thr Leu Ala Pro Ser Arg Pro Leu Leu Val Pro Lys Ala Glu
 420 425 430

Arg Leu Ser Pro Pro Ala Pro Ser Gly Lys Glu Arg Gly Cys Arg Asp
 435 440 445

Trp Gly Asn Leu Gly Asp Glu Gly Lys Arg Arg Lys Lys Lys Gly Thr
 450 455 460

Gly Ser Gly Ala Arg
 465

<210> 137
 <211> 191
 <212> PRT
 <213> Homo sapien

<400> 137

Val Leu Pro Cys Pro Gly Pro Gly Pro Leu Val Thr Ser Cys Phe Pro
 1 5 10 15

Pro Thr Val Ser Pro Tyr Pro His Pro Gly Pro Gly Trp Ser Pro Ala
 20 25 30

His Arg Gly Ala Thr Gly Gly Asn Gly Pro Asp Ser Gly Ala Thr Asp
 35 40 45

Ser Pro Ala Val Gly Asp Asp Asp Arg Glu Gln Val Ala Gly Pro Lys
 50 55 60

Gly Lys Ala Pro Pro Val Pro Ala Pro Ala Arg Glu Ser Gly Asn Arg
 65 70 75 80

Ser Ala Arg Pro Leu His Ser Leu Ser Val Leu Ala Phe Asp Gln Glu

85

90

95

Arg Leu Glu Arg Lys Ile Leu Ala Leu Arg Gln Ala Arg Arg Pro Val
 100 105 110

Pro Pro Glu Val Ala Gln Gln Tyr Gln Asp Ile Met Gln Arg Ser Gln
 115 120 125

Trp Gln Arg Ala Gln Leu Glu Gln Gly Gly Val Gly Ile Arg Arg Glu
 130 135 140

Tyr Ala Ala Gln Leu Glu Arg Gln Leu Gln Phe Tyr Thr Glu Ala Ala
 145 150 155 160

Arg Arg Leu Gly Asn Asp Gly Ser Arg Asp Ala Ala Lys Glu Ala Leu
 165 170 175

Tyr Arg Arg Asn Leu Val Glu Ser Glu Leu Gln Arg Leu Arg Arg
 180 185 190

<210> 138
 <211> 117
 <212> PRT
 <213> Homo sapien

<400> 138

Glu Gly Leu Gly Asp Gly His Leu Glu Gly Glu Gly Leu Gly Asp Gly
 1 5 10 15

His Leu Glu Gly Glu Gly Leu Gly Asp Gly His Leu Glu Gly Glu Gly
 20 25 30

Leu Gly Asp Gly His Leu Ala Gly Asp Gly Leu Gly Asp Gly His Ser
 35 40 45

Pro Gly Gly Leu Trp Ala Val Arg Pro His Pro Lys Pro Pro Phe Pro
 50 55 60

Arg His Pro Phe Ser Glu Tyr Ala Ala Gln Leu Glu Arg Gln Leu Gln
 65 70 75 80

Phe Tyr Thr Glu Ala Ala Arg Arg Leu Gly Asn Asp Gly Ser Arg Asp
 85 90 95

Ala Ala Lys Glu Ala Leu Tyr Arg Arg Asn Leu Val Glu Ser Glu Leu
 100 105 110

Gln Arg Leu Arg Arg
115

<210> 139
<211> 165
<212> PRT
<213> Homo sapien

<400> 139

Arg Val Ser Cys Ser Gly Ser Ala Gly Glu Glu Pro Met Gly Arg Ala
1 5 10 15

Ala Pro Arg Lys Arg Ala Ala Gly Pro Asp Thr Gly Lys Ser Arg His
20 25 30

Ser His Glu Pro Asp Lys Gln Thr Ile Ser Gly Gln Ser Val Leu Asp
35 40 45

Ser Pro Leu Ile Arg Ala Pro Ser Pro Ala Arg Ala Ser Val Ala Ala
50 55 60

Gly Val Gly Asn His Ala Cys Gln Pro Val Cys Ala Pro His Pro Gly
65 70 75 80

Leu Ala Gly Pro Trp Arg Val Leu Phe Ala Gln Pro Arg Gly Val Arg
85 90 95

Pro Leu Ala Arg Pro Gly Ala Gly Arg Val Ala Gly Ala Lys Pro Arg
100 105 110

Gly Pro Leu Gln Ala Leu Tyr Phe Leu Phe Leu Pro Ser Leu Asn Pro
115 120 125

Lys Ala Leu Leu His Pro Lys Glu Ala Thr Glu Ala Gly Arg Ala Thr
130 135 140

Leu Ser Pro Gln Gly Arg Arg Pro Gly Pro Ala Gly Ser Pro Gly Pro
145 150 155 160

Ala His Gly Ile Lys
165

<210> 140
<211> 146
<212> PRT
<213> Homo sapien

<400> 140

Glu Gly Leu Gly Asp Gly His Leu Glu Gly Glu Gly Leu Gly Asp Gly
 1 5 10 15

His Leu Glu Gly Glu Gly Leu Gly Asp Gly His Leu Glu Gly Glu Gly
 20 25 30

Leu Gly Asp Gly His Leu Ala Gly Asp Gly Leu Gly Asp Gly His Ser
 35 40 45

Pro Gly Gly Leu Trp Ala Val Arg Pro His Pro Lys Pro Pro Phe Pro
 50 55 60

Arg His Pro Phe Ser Glu Tyr Ala Ala Gln Leu Glu Arg Gln Leu Gln
 65 70 75 80

Phe Tyr Thr Glu Ala Ala Arg Arg Leu Gly Asn Asp Gly Ser Arg Val
 85 90 95

Ser Trp Ser Arg Ala Gly Trp Ala Leu Gly Ser Gly Gln Gly Gly Ala
 100 105 110

Cys Arg Asp Tyr Leu Leu Asn Ala His Pro Pro Gln Asp Ala Ala Lys
 115 120 125

Glu Ala Leu Tyr Arg Arg Asn Leu Val Glu Ser Glu Leu Gln Arg Leu
 130 135 140

Arg Arg
 145

<210> 141

<211> 165

<212> PRT

<213> Homo sapien

<400> 141

Arg Val Ser Cys Ser Gly Ser Ala Gly Glu Glu Pro Met Gly Arg Ala
 1 5 10 15

Ala Pro Arg Lys Arg Ala Ala Gly Pro Asp Thr Gly Lys Ser Arg His
 20 25 30

Ser His Glu Pro Asp Lys Gln Thr Ile Ser Gly Gln Ser Val Leu Asp
 35 40 45

Ser Pro Leu Ile Arg Ala Pro Ser Pro Ala Arg Ala Ser Val Ala Ala
50 55 60

Gly Val Gly Asn His Ala Cys Gln Pro Val Cys Ala Pro His Pro Gly
65 70 75 80

Leu Ala Gly Pro Trp Arg Val Leu Phe Ala Gln Pro Arg Gly Val Arg
85 90 95

Pro Leu Ala Arg Pro Gly Ala Gly Arg Val Ala Gly Ala Lys Pro Arg
100 105 110

Gly Pro Leu Gln Ala Leu Tyr Phe Leu Phe Leu Pro Ser Leu Asn Pro
115 120 125

Lys Ala Leu Leu His Pro Lys Glu Ala Thr Glu Ala Gly Arg Ala Thr
130 135 140

Leu Ser Pro Gln Gly Arg Arg Pro Gly Pro Ala Gly Ser Pro Gly Pro
145 150 155 160

Ala His Gly Ile Lys
165

<210> 142
<211> 636
<212> PRT
<213> Homo sapien

<400> 142

Met Thr Ser Ser Gly Pro Gly Pro Arg Phe Leu Leu Leu Leu Pro Leu
1 5 10 15

Leu Leu Pro Pro Ala Ala Ser Ala Ser Asp Arg Pro Arg Gly Arg Asp
20 25 30

Pro Val Asn Pro Glu Lys Leu Leu Val Ile Thr Val Ala Thr Ala Glu
35 40 45

Thr Glu Gly Tyr Leu Arg Phe Leu Arg Ser Ala Glu Phe Phe Asn Tyr
50 55 60

Thr Val Arg Thr Leu Gly Leu Gly Glu Glu Trp Arg Gly Gly Asp Val
65 70 75 80

Ala Arg Thr Val Gly Gly Gly Gln Lys Val Arg Trp Leu Lys Lys Glu
85 90 95

Met Glu Lys Tyr Ala Asp Arg Glu Asp Met Ile Ile Met Phe Val Asp
100 105 110

Ser Tyr Asp Val Ile Leu Ala Gly Ser Pro Thr Glu Leu Leu Lys Lys
115 120 125

Phe Val Gln Ser Gly Ser Arg Leu Leu Phe Ser Ala Glu Ser Phe Cys
130 135 140

Trp Pro Glu Trp Gly Leu Ala Glu Gln Tyr Pro Glu Val Gly Thr Gly
145 150 155 160

Lys Arg Phe Leu Asn Ser Gly Gly Phe Ile Gly Phe Ala Thr Thr Ile
165 170 175

His Gln Ile Val Arg Gln Trp Lys Tyr Lys Asp Asp Asp Asp Asp Gln
180 185 190

Leu Phe Tyr Thr Arg Leu Tyr Leu Asp Pro Gly Leu Arg Glu Lys Leu
195 200 205

Ser Leu Asn Leu Asp His Lys Ser Arg Ile Phe Gln Asn Leu Asn Gly
210 215 220

Ala Leu Asp Glu Val Val Leu Lys Phe Asp Arg Asn Arg Val Arg Ile
225 230 235 240

Arg Asn Val Ala Tyr Asp Thr Leu Pro Ile Val Val His Gly Asn Gly
245 250 255

Pro Thr Lys Leu Gln Leu Asn Tyr Leu Gly Asn Tyr Val Pro Asn Gly
260 265 270

Trp Thr Pro Glu Gly Gly Cys Gly Phe Cys Asn Gln Asp Arg Arg Thr
275 280 285

Leu Pro Gly Gly Gln Pro Pro Pro Arg Val Phe Leu Ala Val Phe Val
290 295 300

Glu Gln Pro Thr Pro Phe Leu Pro Arg Phe Leu Gln Arg Leu Leu Leu
305 310 315 320

Leu Asp Tyr Pro Pro Asp Arg Val Thr Leu Phe Leu His Asn Asn Glu
325 330 335

Val Phe His Glu Pro His Ile Ala Asp Ser Trp Pro Gln Leu Gln Asp
340 345 350

His Phe Ser Ala Val Lys Leu Val Gly Pro Glu Glu Ala Leu Ser Pro
355 360 365

Gly Glu Ala Arg Asp Met Ala Met Asp Leu Cys Arg Gln Asp Pro Glu
370 375 380

Cys Glu Phe Tyr Phe Ser Leu Asp Ala Asp Ala Val Leu Thr Asn Leu
385 390 395 400

Gln Thr Leu Arg Ile Leu Ile Glu Glu Asn Arg Lys Val Ile Ala Pro
405 410 415

Met Leu Ser Arg His Gly Lys Leu Trp Ser Asn Phe Trp Gly Ala Leu
420 425 430

Ser Pro Asp Glu Tyr Tyr Ala Arg Ser Glu Asp Tyr Val Glu Leu Val
435 440 445

Gln Arg Lys Arg Val Gly Val Trp Asn Val Pro Tyr Ile Ser Gln Ala
450 455 460

Tyr Val Ile Arg Gly Asp Thr Leu Arg Met Glu Leu Pro Gln Arg Asp
465 470 475 480

Val Phe Ser Gly Ser Asp Thr Asp Pro Asp Met Ala Phe Cys Lys Ser
485 490 495

Phe Arg Asp Lys Gly Ile Phe Leu His Leu Ser Asn Gln His Glu Phe
500 505 510

Gly Arg Leu Leu Ala Thr Ser Arg Tyr Asp Thr Glu His Leu His Pro
515 520 525

Asp Leu Trp Gln Ile Phe Asp Asn Pro Val Asp Trp Lys Glu Gln Tyr
530 535 540

Ile His Glu Asn Tyr Ser Arg Ala Leu Glu Gly Glu Gly Ile Val Glu
545 550 555 560

Gln Pro Cys Pro Asp Val Tyr Trp Phe Pro Leu Leu Ser Glu Gln Met
565 570 575

235/383

Cys Asp Glu Leu Val Ala Glu Met Glu His Tyr Gly Gln Trp Ser Gly
580 585 590

Gly Arg His Glu Thr Ala Leu Gln Glu Cys Leu Met Pro Val Glu Leu
595 600 605

Cys Pro Ala Val Ser Ser Ser His His Thr Ala Ser Lys Ala Ala Met
610 615 620

Ser Ser Leu Gly Ala Ile Glu Ala Thr Gly Lys Pro
625 630 635

<210> 143

<211> 682

<212> PRT

<213> Homo sapien

<400> 143

Met Thr Ser Ser Gly Pro Gly Pro Arg Phe Leu Leu Leu Leu Pro Leu
1 5 10 15

Leu Leu Pro Pro Ala Ala Ser Ala Ser Asp Arg Pro Arg Gly Arg Asp
20 25 30

Pro Val Asn Pro Glu Lys Leu Leu Val Ile Thr Val Ala Thr Ala Glu
35 40 45

Thr Glu Gly Tyr Leu Arg Phe Leu Arg Ser Ala Glu Phe Phe Asn Tyr
50 55 60

Thr Val Arg Thr Leu Gly Leu Gly Glu Glu Trp Arg Gly Gly Asp Val
65 70 75 80

Ala Arg Thr Val Gly Gly Gly Gln Lys Val Arg Trp Leu Lys Lys Glu
85 90 95

Met Glu Lys Tyr Ala Asp Arg Glu Asp Met Ile Ile Met Phe Val Asp
100 105 110

Ser Tyr Asp Val Ile Leu Ala Gly Ser Pro Thr Glu Leu Leu Lys Lys
115 120 125

Phe Val Gln Ser Gly Ser Arg Leu Leu Phe Ser Ala Glu Ser Phe Cys
130 135 140

Trp Pro Glu Trp Gly Leu Ala Glu Gln Tyr Pro Glu Val Gly Thr Gly
145 150 155 160

Lys Arg Phe Leu Asn Ser Gly Gly Phe Ile Gly Phe Ala Thr Thr Ile
 165 170 175

His Gln Ile Val Arg Gln Trp Lys Tyr Lys Asp Asp Asp Asp Asp Gln
 180 185 190

Leu Phe Tyr Thr Arg Leu Tyr Leu Asp Pro Gly Leu Arg Glu Lys Leu
 195 200 205

Ser Leu Asn Leu Asp His Lys Ser Arg Ile Phe Gln Asn Leu Asn Gly
 210 215 220

Ala Leu Asp Glu Val Val Leu Lys Phe Asp Arg Asn Arg Val Arg Ile
 225 230 235 240

Arg Asn Val Ala Tyr Asp Thr Leu Pro Ile Val Val His Gly Asn Gly
 245 250 255

Pro Thr Lys Leu Gln Leu Asn Tyr Leu Gly Asn Tyr Val Pro Asn Gly
 260 265 270

Trp Thr Pro Glu Gly Gly Cys Gly Phe Cys Asn Gln Asp Arg Arg Thr
 275 280 285

Leu Pro Gly Gly Gln Pro Pro Pro Arg Val Phe Leu Ala Val Phe Val
 290 295 300

Glu Gln Pro Thr Pro Phe Leu Pro Arg Phe Leu Gln Arg Leu Leu Leu
 305 310 315 320

Leu Asp Tyr Pro Pro Asp Arg Val Thr Leu Phe Leu His Asn Asn Glu
 325 330 335

Val Phe His Glu Pro His Ile Ala Asp Ser Trp Pro Gln Leu Gln Asp
 340 345 350

His Phe Ser Ala Val Lys Leu Val Gly Pro Glu Glu Ala Leu Ser Pro
 355 360 365

Gly Glu Ala Arg Asp Met Ala Met Asp Leu Cys Arg Gln Asp Pro Glu
 370 375 380

Cys Glu Phe Tyr Phe Ser Leu Asp Ala Asp Ala Val Leu Thr Asn Leu
 385 390 395 400

Gln Thr Leu Arg Ile Leu Ile Glu Glu Asn Arg Lys Val Ile Ala Pro
 405 410 415

Met Leu Ser Arg His Gly Lys Leu Trp Ser Asn Phe Trp Gly Ala Leu
 420 425 430

Ser Pro Asp Glu Tyr Tyr Ala Arg Ser Glu Asp Tyr Val Glu Leu Val
 435 440 445

Gln Arg Lys Arg Val Gly Val Trp Asn Val Pro Tyr Ile Ser Gln Ala
 450 455 460

Tyr Val Ile Arg Gly Asp Thr Leu Arg Met Glu Leu Pro Gln Arg Asp
 465 470 475 480

Val Phe Ser Gly Ser Asp Thr Asp Pro Asp Met Ala Phe Cys Lys Ser
 485 490 495

Phe Arg Asp Lys Gly Ile Phe Leu His Leu Ser Asn Gln His Glu Phe
 500 505 510

Gly Arg Leu Leu Ala Thr Ser Arg Tyr Asp Thr Glu His Leu His Pro
 515 520 525

Asp Leu Trp Gln Ile Phe Asp Asn Pro Val Asp Trp Lys Glu Gln Tyr
 530 535 540

Ile His Glu Asn Tyr Ser Arg Ala Leu Glu Gly Glu Gly Ile Val Glu
 545 550 555 560

Gln Pro Cys Pro Asp Val Tyr Trp Phe Pro Leu Leu Ser Glu Gln Met
 565 570 575

Cys Asp Glu Leu Val Ala Glu Met Glu His Tyr Gly Gln Trp Ser Gly
 580 585 590

Gly Arg His Glu Val Arg Ala Trp Ala Arg Arg Ala Glu Ala Phe Pro
 595 600 605

Glu Glu Glu Val Gln Asp Leu Val Asn Lys Gln Trp Asn Gln Glu Asn
 610 615 620

Gly Ser Lys Glu Gly Phe Pro Gly Gly Arg Gln Thr Leu Gly Ser Gln
 625 630 635 640

238/383

Leu His Ser Phe Met Tyr Ser Arg Asn Ile Tyr Cys Trp Ala Gln Trp
 645 650 655

Leu Met Pro Val Ile Leu Ala Leu Trp Glu Ala Glu Ala Gly Gly Leu
 660 665 670

Leu Glu Gln Gly Glu Phe Glu Ala Ser Leu
 675 680

<210> 144

<211> 654

<212> PRT

<213> Homo sapien

<400> 144

Met Thr Ser Ser Gly Pro Gly Pro Arg Phe Leu Leu Leu Leu Pro Leu
 1 5 10 15

Leu Leu Pro Pro Ala Ala Ser Ala Ser Asp Arg Pro Arg Gly Arg Asp
 20 25 30

Pro Val Asn Pro Glu Lys Leu Leu Val Ile Thr Val Ala Thr Ala Glu
 35 40 45

Thr Glu Gly Tyr Leu Arg Phe Leu Arg Ser Ala Glu Phe Phe Asn Tyr
 50 55 60

Thr Val Arg Thr Leu Gly Leu Gly Glu Glu Trp Arg Gly Gly Asp Val
 65 70 75 80

Ala Arg Thr Val Gly Gly Gly Gln Lys Val Arg Trp Leu Lys Lys Glu
 85 90 95

Met Glu Lys Tyr Ala Asp Arg Glu Asp Met Ile Ile Met Phe Val Asp
 100 105 110

Ser Tyr Asp Val Ile Leu Ala Gly Ser Pro Thr Glu Leu Leu Lys Lys
 115 120 125

Phe Val Gln Ser Gly Ser Arg Leu Leu Phe Ser Ala Glu Ser Phe Cys
 130 135 140

Trp Pro Glu Trp Gly Leu Ala Glu Gln Tyr Pro Glu Val Gly Thr Gly
 145 150 155 160

Lys Arg Phe Leu Asn Ser Gly Gly Phe Ile Gly Phe Ala Thr Thr Ile
 165 170 175

His Gln Ile Val Arg Gln Trp Lys Tyr Lys Asp Asp Asp Asp Asp Gln
 180 185 190

Leu Phe Tyr Thr Arg Leu Tyr Leu Asp Pro Gly Leu Arg Glu Lys Leu
 195 200 205

Ser Leu Asn Leu Asp His Lys Ser Arg Ile Phe Gln Asn Leu Asn Gly
 210 215 220

Ala Leu Asp Glu Val Val Leu Lys Phe Asp Arg Asn Arg Val Arg Ile
 225 230 235 240

Arg Asn Val Ala Tyr Asp Thr Leu Pro Ile Val Val His Gly Asn Gly
 245 250 255

Pro Thr Lys Leu Gln Leu Asn Tyr Leu Gly Asn Tyr Val Pro Asn Gly
 260 265 270

Trp Thr Pro Glu Gly Gly Cys Gly Phe Cys Asn Gln Asp Arg Arg Thr
 275 280 285

Leu Pro Gly Gly Gln Pro Pro Pro Arg Val Phe Leu Ala Val Phe Val
 290 295 300

Glu Gln Pro Thr Pro Phe Leu Pro Arg Phe Leu Gln Arg Leu Leu Leu
 305 310 315 320

Leu Asp Tyr Pro Pro Asp Arg Val Thr Leu Phe Leu His Asn Asn Glu
 325 330 335

Val Phe His Glu Pro His Ile Ala Asp Ser Trp Pro Gln Leu Gln Asp
 340 345 350

His Phe Ser Ala Val Lys Leu Val Gly Pro Glu Glu Ala Leu Ser Pro
 355 360 365

Gly Glu Ala Arg Asp Met Ala Met Asp Leu Cys Arg Gln Asp Pro Glu
 370 375 380

Cys Glu Phe Tyr Phe Ser Leu Asp Ala Asp Ala Val Leu Thr Asn Leu
 385 390 395 400

Gln Thr Leu Arg Ile Leu Ile Glu Glu Asn Arg Lys Val Ile Ala Pro
 405 410 415

Met Leu Ser Arg His Gly Lys Leu Trp Ser Asn Phe Trp Gly Ala Leu
 420 425 430

Ser Pro Asp Glu Tyr Tyr Ala Arg Ser Glu Asp Tyr Val Glu Leu Val
 435 440 445

Gln Arg Lys Arg Val Gly Val Trp Asn Val Pro Tyr Ile Ser Gln Ala
 450 455 460

Tyr Val Ile Arg Gly Asp Thr Leu Arg Met Glu Leu Pro Gln Arg Asp
 465 470 475 480

Val Phe Ser Gly Ser Asp Thr Asp Pro Asp Met Ala Phe Cys Lys Ser
 485 490 495

Phe Arg Asp Lys Gly Ile Phe Leu His Leu Ser Asn Gln His Glu Phe
 500 505 510

Gly Arg Leu Leu Ala Thr Ser Arg Tyr Asp Thr Glu His Leu His Pro
 515 520 525

Asp Leu Trp Gln Ile Phe Asp Asn Pro Val Asp Trp Lys Glu Gln Tyr
 530 535 540

Ile His Glu Asn Tyr Ser Arg Ala Leu Glu Gly Glu Gly Ile Val Glu
 545 550 555 560

Gln Pro Cys Pro Asp Val Tyr Trp Phe Pro Leu Leu Ser Glu Gln Met
 565 570 575

Cys Asp Glu Leu Val Ala Glu Met Glu His Tyr Gly Gln Trp Ser Gly
 580 585 590

Gly Arg His Glu Trp Glu Gly Thr Asn Gly Ala Gly Pro His Met Lys
 595 600 605

Gly Gly Pro Gly Gln Val Ile Gly Ser Leu Ala Asp Asn Leu Ala Ala
 610 615 620

Thr Gly Gly Gly Lys Gly Pro Ala Lys Ser Gly Pro Asn His Gln His
 625 630 635 640

Arg Ala Arg Gly Gln Thr Gly Thr Pro Lys Gly Asp Thr Gly
 645 650

<210> 145
 <211> 669
 <212> PRT
 <213> Homo sapien

<220>
 <221> MISC_FEATURE
 <222> (613)..(613)
 <223> X=any amino acid

<400> 145

Arg Arg Ser Gln Asp Pro Gly Cys Cys Leu Gly Pro Leu Pro Thr Met
 1 5 10 15

Thr Ser Ser Gly Pro Gly Pro Arg Phe Leu Leu Leu Leu Pro Leu Leu
 20 25 30

Leu Pro Pro Ala Ala Ser Ala Ser Asp Arg Pro Arg Gly Arg Asp Pro
 35 40 45

Val Asn Pro Glu Lys Leu Leu Val Ile Thr Val Ala Thr Ala Glu Thr
 50 55 60

Glu Gly Tyr Leu Arg Phe Leu Arg Ser Ala Glu Phe Phe Asn Tyr Thr
 65 70 75 80

Val Arg Thr Leu Gly Leu Gly Glu Glu Trp Arg Gly Gly Asp Val Ala
 85 90 95

Arg Thr Val Gly Gly Gly Gln Lys Val Arg Trp Leu Lys Lys Glu Met
 100 105 110

Glu Lys Tyr Ala Asp Arg Glu Asp Met Ile Ile Met Phe Val Asp Ser
 115 120 125

Tyr Asp Val Ile Leu Ala Gly Ser Pro Thr Glu Leu Leu Lys Lys Phe
 130 135 140

Val Gln Ser Gly Ser Arg Leu Leu Phe Ser Ala Glu Ser Phe Cys Trp
 145 150 155 160

Pro Glu Trp Gly Leu Ala Glu Gln Tyr Pro Glu Val Gly Thr Gly Lys
 165 170 175

Arg Phe Leu Asn Ser Gly Gly Phe Ile Gly Phe Ala Thr Thr Ile His
 180 185 190

242/383

Gln Ile Val Arg Gln Trp Lys Tyr Lys Asp Asp Asp Asp Gln Leu
 195 200 205

Phe Tyr Thr Arg Leu Tyr Leu Asp Pro Gly Leu Arg Glu Lys Leu Ser
 210 215 220

Leu Asn Leu Asp His Lys Ser Arg Ile Phe Gln Asn Leu Asn Gly Ala
 225 230 235 240

Leu Asp Glu Val Val Leu Lys Phe Asp Arg Asn Arg Val Arg Ile Arg
 245 250 255

Asn Val Ala Tyr Asp Thr Leu Pro Ile Val Val His Gly Asn Gly Pro
 260 265 270

Thr Lys Leu Gln Leu Asn Tyr Leu Gly Asn Tyr Val Pro Asn Gly Trp
 275 280 285

Thr Pro Glu Gly Gly Cys Gly Phe Cys Asn Gln Asp Arg Arg Thr Leu
 290 295 300

Pro Gly Gly Gln Pro Pro Pro Arg Val Phe Leu Ala Val Phe Val Glu
 305 310 315 320

Gln Pro Thr Pro Phe Leu Pro Arg Phe Leu Gln Arg Leu Leu Leu Leu
 325 330 335

Asp Tyr Pro Pro Asp Arg Val Thr Leu Phe Leu His Asn Asn Glu Val
 340 345 350

Phe His Glu Pro His Ile Ala Asp Ser Trp Pro Gln Leu Gln Asp His
 355 360 365

Phe Ser Ala Val Lys Leu Val Gly Pro Glu Glu Ala Leu Ser Pro Gly
 370 375 380

Glu Ala Arg Asp Met Ala Met Asp Leu Cys Arg Gln Asp Pro Glu Cys
 385 390 395 400

Glu Phe Tyr Phe Ser Leu Asp Ala Asp Ala Val Leu Thr Asn Leu Gln
 405 410 415

Thr Leu Arg Ile Leu Ile Glu Glu Asn Arg Lys Val Ile Ala Pro Met
 420 425 430

Leu Ser Arg His Gly Lys Leu Trp Ser Asn Phe Trp Gly Ala Leu Ser

243/383

435 440 445
 Pro Asp Glu Tyr Tyr Ala Arg Ser Glu Asp Tyr Val Glu Leu Val Gln
 450 455 460
 Arg Lys Arg Val Gly Val Trp Asn Val Pro Tyr Ile Ser Gln Ala Tyr
 465 470 475 480
 Val Ile Arg Gly Asp Thr Leu Arg Met Glu Leu Pro Gln Arg Asp Val
 485 490 495
 Phe Ser Gly Ser Asp Thr Asp Pro Asp Met Ala Phe Cys Lys Ser Phe
 500 505 510
 Arg Asp Lys Gly Ile Phe Leu His Leu Ser Asn Gln His Glu Phe Gly
 515 520 525
 Arg Leu Leu Ala Thr Ser Arg Tyr Asp Thr Glu His Leu His Pro Asp
 530 535 540
 Leu Trp Gln Ile Phe Asp Asn Pro Val Asp Trp Lys Glu Gln Tyr Ile
 545 550 555 560
 His Glu Asn Tyr Ser Arg Ala Leu Glu Gly Glu Gly Ile Val Glu Gln
 565 570 575
 Pro Cys Pro Asp Val Tyr Trp Phe Pro Leu Leu Ser Glu Gln Met Cys
 580 585 590
 Asp Glu Leu Val Ala Glu Met Glu His Tyr Gly Gln Trp Ser Gly Gly
 595 600 605
 Arg His Glu Trp Xaa Gly Thr Asn Gly Ala Gly Pro His Met Lys Gly
 610 615 620
 Gly Pro Gly Gln Val Ile Gly Ser Leu Ala Asp Asn Leu Ala Ala Thr
 625 630 635 640
 Gly Gly Gly Lys Gly Pro Ala Lys Ser Gly Pro Asn His Gln His Arg
 645 650 655
 Ala Arg Gly Gln Thr Gly Thr Pro Lys Gly Asp Thr Gly
 660 665

<210> 146

<211> 411

<212> PRT

<213> Homo sapien

<400> 146

Met Gln Gly Pro Tyr Val Gln Gly Leu Gly Tyr Pro Glu Gly Arg Arg
 1 5 10 15

Thr Ser Arg Asp Glu Leu Gly Arg Ile Trp Gly Ala Val Leu Pro Ala
 20 25 30

Asp Arg Gly Val Gly Ala Ser Arg Gly Gly Val Trp Asn Val Pro Tyr
 35 40 45

Ile Ser Gln Ala Tyr Val Ile Arg Gly Asp Thr Leu Arg Met Glu Leu
 50 55 60

Pro Gln Arg Asp Val Phe Ser Gly Ser Asp Thr Asp Pro Asp Met Ala
 65 70 75 80

Phe Cys Lys Ser Phe Arg Asp Lys Val Ser Ala Gly Ala Arg Ser Gly
 85 90 95

Leu Gly Ala Val Pro Gln Thr Pro Gly Ile Ala Cys Ile Thr Asp Thr
 100 105 110

Pro Thr Pro Leu Thr Gly Ile Phe Leu His Leu Ser Asn Gln His Glu
 115 120 125

Phe Gly Arg Leu Leu Ala Thr Ser Arg Tyr Asp Thr Glu His Leu His
 130 135 140

Pro Asp Leu Trp Gln Ile Phe Asp Asn Pro Val Val Ser Gly Asp Pro
 145 150 155 160

Ser Pro Glu His Thr Gly Ser Pro Pro Cys Ala Lys Glu Asp Thr Lys
 165 170 175

Arg Asp Gly Cys Cys Gln Arg Arg Thr Leu Ser Gly Arg Gly Arg Ser
 180 185 190

Pro Gly Gly Trp Glu Arg Gly Gly His Arg Ser Asp Val Pro Pro Thr
 195 200 205

Leu Ser Gln Asp Trp Lys Glu Gln Tyr Ile His Glu Asn Tyr Ser Arg
 210 215 220

245/383

Ala Leu Glu Gly Glu Gly Ile Val Glu Gln Pro Cys Pro Asp Val Tyr
 225 230 235 240

Trp Phe Pro Leu Leu Ser Glu Gln Met Cys Asp Glu Leu Val Ala Glu
 245 250 255

Met Glu His Tyr Gly Gln Trp Ser Gly Gly Arg His Glu Asp Ser Arg
 260 265 270

Leu Ala Gly Gly Tyr Glu Asn Val Pro Thr Val Asp Ile His Met Lys
 275 280 285

Gln Val Gly Tyr Glu Asp Gln Trp Leu Gln Leu Leu Arg Thr Tyr Val
 290 295 300

Gly Pro Met Thr Glu Ser Leu Phe Pro Gly Tyr His Thr Lys Ala Arg
 305 310 315 320

Ala Val Met Asn Phe Val Val Arg Tyr Arg Pro Asp Glu Gln Pro Ser
 325 330 335

Leu Arg Pro His His Asp Ser Ser Thr Phe Thr Leu Asn Val Ala Leu
 340 345 350

Asn His Lys Gly Leu Asp Tyr Glu Gly Gly Gly Cys Arg Phe Leu Arg
 355 360 365

Tyr Asp Cys Val Ile Ser Ser Pro Arg Lys Gly Trp Ala Leu Leu His
 370 375 380

Pro Gly Arg Leu Thr His Tyr His Glu Gly Leu Pro Thr Thr Trp Gly
 385 390 395 400

Thr Arg Tyr Ile Met Val Ser Phe Val Asp Pro
 405 410

<210> 147
 <211> 255
 <212> PRT
 <213> Homo sapien

<400> 147

Val Gly Thr Pro Arg Pro Glu His Thr Gly Ser Pro Pro Cys Ala Lys
 1 5 10 15

Glu Asp Thr Lys Arg Asp Gly Cys Cys Gln Arg Arg Thr Leu Ser Gly
 20 25 30

Arg Gly Arg Ser Pro Gly Gly Trp Glu Arg Gly Gly His Arg Ser Asp
 35 40 45
 Val Pro Pro Thr Leu Ser Gln Asp Trp Lys Glu Gln Tyr Ile His Glu
 50 55 60
 Asn Tyr Ser Arg Ala Leu Glu Gly Glu Gly Ile Val Glu Gln Pro Cys
 65 70 75 80
 Pro Asp Val Tyr Trp Phe Pro Leu Leu Ser Glu Gln Met Cys Asp Glu
 85 90 95
 Leu Val Ala Glu Met Glu His Tyr Gly Gln Trp Ser Gly Gly Arg His
 100 105 110
 Glu Asp Ser Arg Leu Ala Gly Gly Tyr Glu Asn Val Pro Thr Val Asp
 115 120 125
 Ile His Met Lys Gln Val Gly Tyr Glu Asp Gln Trp Leu Gln Leu Leu
 130 135 140
 Arg Thr Tyr Val Gly Pro Met Thr Glu Ser Leu Phe Pro Gly Tyr His
 145 150 155 160
 Thr Lys Ala Arg Ala Val Met Asn Phe Val Val Arg Tyr Arg Pro Asp
 165 170 175
 Glu Gln Pro Ser Leu Arg Pro His His Asp Ser Ser Thr Phe Thr Leu
 180 185 190
 Asn Val Ala Leu Asn His Lys Gly Leu Asp Tyr Glu Gly Gly Gly Cys
 195 200 205
 Arg Phe Leu Arg Tyr Asp Cys Val Ile Ser Ser Pro Arg Lys Gly Trp
 210 215 220
 Ala Leu Leu His Pro Gly Arg Leu Thr His Tyr His Glu Gly Leu Pro
 225 230 235 240
 Thr Thr Trp Gly Thr Arg Tyr Ile Met Val Ser Phe Val Asp Pro
 245 250 255

<210> 148

<211> 312

<212> PRT

<213> Homo sapien

<400> 148

Met Arg Ser Pro Glu Leu Ala Leu Pro Arg Gly Met Gln Pro Thr Glu
1 5 10 15

Phe Phe Gln Ser Leu Gly Gly Asp Gly Glu Arg Asn Val Gln Ile Glu
20 25 30

Met Ala His Gly Thr Thr Thr Leu Ala Phe Lys Phe Gln His Gly Val
35 40 45

Ile Ala Ala Val Asp Ser Arg Ala Ser Ala Gly Ser Tyr Ile Ser Ala
50 55 60

Leu Arg Val Asn Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr
65 70 75 80

Met Ser Gly Cys Ala Ala Asp Cys Gln Tyr Trp Glu Arg Leu Leu Ala
85 90 95

Lys Glu Cys Arg Leu Tyr Tyr Leu Arg Asn Gly Glu Arg Ile Ser Val
100 105 110

Ser Ala Ala Ser Lys Leu Leu Ser Asn Met Met Cys Gln Tyr Arg Gly
115 120 125

Met Gly Leu Ser Met Gly Ser Met Ile Cys Gly Trp Asp Lys Lys Gly
130 135 140

Pro Gly Leu Tyr Tyr Val Asp Glu His Gly Thr Arg Leu Ser Gly Asn
145 150 155 160

Met Phe Ser Thr Gly Ser Gly Asn Thr Tyr Ala Tyr Gly Val Met Asp
165 170 175

Ser Gly Tyr Arg Pro Asn Leu Ser Pro Glu Glu Ala Tyr Asp Leu Gly
180 185 190

Arg Arg Ala Ile Ala Tyr Ala Thr His Arg Asp Ser Tyr Ser Gly Gly
195 200 205

Val Val Asn Met Ser Thr Val Ser Ser Trp Ser Gly Pro Leu Glu Arg
210 215 220

Pro Met Ser Cys Pro Val Cys Pro Ser Gly Ser Ala Ser Ile Ala Ala

225 230 235 240

Gly Ala Gly Gly Arg Pro Gly Arg Thr Cys Gly Pro Pro Gly His Thr
 245 250 255

Leu Ser Pro Gly Lys Lys Gly Val Val Cys Gln Gln Lys Val Val Ser
 260 265 270

Thr Ser Gly Lys His Met Gly Arg Tyr Lys Ser Arg Val Cys Ala Ala
 275 280 285

Lys Met Ile Ile Ile Gly Gly Gly Ser Thr Pro Tyr Pro Tyr Asn Gly
 290 295 300

Ser Arg Val His Thr Ser Tyr Tyr
305 310

<210> 149
<211> 299
<212> PRT
<213> Homo sapien

<400> 149

Leu Ser Phe Ser Arg Lys Arg Gln Gly Asp Val Glu Lys Ser Leu Val
1 5 10 15

Pro Ser Pro Ser Ile Cys Gly Phe Arg Phe His Phe Leu Leu Arg Glu
 20 25 30

Arg Thr Asp Leu Trp Val Leu Gly Gly His Gly Ala Thr Arg Cys Met
 35 40 45

Arg Ser Pro Arg Gly Gln Arg Pro Glu Ser Ala Leu Pro Val Ala Gly
50 55 60

Ser Gly Arg Arg Ser Asp Pro Gly His Tyr Ser Phe Ser Met Arg Ser
65 70 75 80

Pro Glu Leu Ala Leu Pro Arg Gly Met Gln Pro Thr Glu Phe Phe Gln
 85 90 95

Ser Leu Gly Gly Asp Gly Glu Arg Asn Val Gln Ile Glu Met Ala His
 100 105 110

Gly Thr Thr Thr Leu Ala Phe Lys Phe Gln His Gly Val Ile Ala Ala
115 120 125

Val Asp Ser Arg Ala Ser Ala Gly Ser Tyr Ile Ser Ala Leu Arg Val
 130 135 140

Asn Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr Met Ser Gly
 145 150 155 160

Cys Ala Ala Asp Cys Gln Tyr Trp Glu Arg Leu Leu Ala Lys Glu Cys
 165 170 175

Arg Leu Tyr Tyr Leu Arg Asn Gly Glu Arg Ile Ser Val Ser Ala Ala
 180 185 190

Ser Lys Leu Leu Ser Asn Met Met Cys Gln Tyr Arg Gly Met Gly Leu
 195 200 205

Ser Met Gly Ser Met Ile Cys Gly Trp Asp Lys Lys Gly Pro Gly Leu
 210 215 220

Tyr Tyr Val Asp Glu His Gly Thr Arg Leu Ser Gly Asn Met Phe Ser
 225 230 235 240

Thr Gly Ser Gly Asn Thr Tyr Ala Tyr Gly Val Met Asp Ser Gly Tyr
 245 250 255

Arg Pro Asn Leu Ser Pro Glu Glu Ala Tyr Asp Leu Gly Arg Arg Ala
 260 265 270

Ile Ala Tyr Ala Thr His Arg Asp Ser Tyr Ser Gly Gly Val Val Asn
 275 280 285

Met Ser Thr Val Ser Ser Trp Ser Arg Ala Thr
 290 295

<210> 150

<211> 274

<212> PRT

<213> Homo sapien

<400> 150

Met Arg Ser Pro Glu Leu Ala Leu Pro Arg Gly Met Gln Pro Thr Glu
 1 5 10 15

Phe Phe Gln Ser Leu Gly Gly Asp Gly Glu Arg Asn Val Gln Ile Glu
 20 25 30

Met Ala His Gly Thr Thr Thr Leu Ala Phe Lys Phe Gln His Gly Val

250/383

Ile Ala Ala Val Asp Ser Arg Ala Ser Ala Gly Ser Tyr Ile Ser Ala
50 55 60

Leu Arg Val Asn Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr
65 70 75 80

Met Ser Gly Cys Ala Ala Asp Cys Gln Tyr Trp Glu Arg Leu Leu Ala
85 90 95

Lys Glu Cys Arg Leu Tyr Tyr Leu Arg Asn Gly Glu Arg Ile Ser Val
100 105 110

Ser Ala Ala Ser Lys Leu Leu Ser Asn Met Met Cys Gln Tyr Arg Gly
115 120 125

Met Gly Leu Ser Met Gly Ser Met Ile Cys Gly Trp Asp Lys Lys Gly
130 135 140

Pro Gly Leu Tyr Tyr Val Asp Glu His Gly Thr Arg Leu Ser Gly Asn
145 150 155 160

Met Phe Ser Thr Gly Ser Gly Asn Thr Tyr Ala Tyr Gly Val Met Asp
165 170 175

Ser Gly Tyr Arg Pro Asn Leu Ser Pro Glu Glu Ala Tyr Asp Leu Gly
180 185 190

Arg Arg Ala Ile Ala Tyr Ala Thr His Arg Asp Ser Tyr Ser Gly Gly
195 200 205

Val Val Asn Ile Pro Glu Asp Gly Gly Asp Ser Glu Arg Pro Phe Gly
210 215 220

Arg Ala Ser Arg Asp His Gln Gly Gly Gly Gly Arg Pro Arg Gly Gly
225 230 235 240

Ser Gly Thr Pro Phe Arg Lys Ser Arg Lys Val Ser Arg Gly Gly Cys
245 250 255

Leu Asn Gln Trp Pro Lys Lys Gly Pro Ala Ala Tyr Trp Arg Ser Ser
260 265 270

Thr Tyr

<210> 151
 <211> 294
 <212> PRT
 <213> Homo sapien

<400> 151

Leu Ser Phe Ser Arg Lys Arg Gln Gly Asp Val Glu Lys Ser Leu Val
 1 5 10 15

Pro Ser Pro Ser Ile Cys Gly Phe Arg Phe His Phe Leu Leu Arg Glu
 20 25 30

Arg Thr Asp Leu Trp Val Leu Gly Gly His Gly Ala Thr Arg Cys Met
 35 40 45

Arg Ser Pro Arg Gly Gln Arg Pro Glu Ser Ala Leu Pro Val Ala Gly
 50 55 60

Ser Gly Arg Arg Ser Asp Pro Gly His Tyr Ser Phe Ser Met Arg Ser
 65 70 75 80

Pro Glu Leu Ala Leu Pro Arg Gly Met Gln Pro Thr Glu Phe Phe Gln
 85 90 95

Ser Leu Gly Gly Asp Gly Glu Arg Asn Val Gln Ile Glu Met Ala His
 100 105 110

Gly Thr Thr Thr Leu Ala Phe Lys Phe Gln His Gly Val Ile Ala Ala
 115 120 125

Val Asp Ser Arg Ala Ser Ala Gly Ser Tyr Ile Ser Ala Leu Arg Val
 130 135 140

Asn Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr Met Ser Gly
 145 150 155 160

Cys Ala Ala Asp Cys Gln Tyr Trp Glu Arg Leu Leu Ala Lys Glu Cys
 165 170 175

Arg Leu Tyr Tyr Leu Arg Asn Gly Glu Arg Ile Ser Val Ser Ala Ala
 180 185 190

Ser Lys Leu Leu Ser Asn Met Met Cys Gln Tyr Arg Gly Met Gly Leu
 195 200 205

252/383

Ser Met Gly Ser Met Ile Cys Gly Trp Asp Lys Lys Gly Pro Gly Leu
 210 215 220

Tyr Tyr Val Asp Glu His Gly Thr Arg Leu Ser Gly Asn Met Phe Ser
 225 230 235 240

Thr Gly Ser Gly Asn Thr Tyr Ala Tyr Gly Val Met Asp Ser Gly Tyr
 245 250 255

Arg Pro Asn Leu Ser Pro Glu Glu Ala Tyr Asp Leu Gly Arg Arg Ala
 260 265 270

Ile Ala Tyr Ala Thr His Arg Asp Ser Tyr Ser Gly Gly Val Val Asn
 275 280 285

Ile Pro Glu Glu Trp Trp
 290

<210> 152
 <211> 237
 <212> PRT
 <213> Homo sapien

<400> 152

Met Arg Ser Pro Glu Leu Ala Leu Pro Arg Gly Met Gln Pro Thr Glu
 1 5 10 15

Phe Phe Gln Ser Leu Gly Gly Asp Gly Glu Arg Asn Val Gln Ile Glu
 20 25 30

Met Ala His Gly Thr Thr Thr Leu Ala Phe Lys Phe Gln His Gly Val
 35 40 45

Ile Ala Ala Val Asp Ser Arg Ala Ser Ala Gly Ser Tyr Ile Ser Ala
 50 55 60

Leu Arg Val Asn Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr
 65 70 75 80

Met Ser Gly Cys Ala Ala Asp Cys Gln Tyr Trp Glu Arg Leu Leu Ala
 85 90 95

Lys Glu Cys Arg Leu Tyr Tyr Leu Arg Asn Gly Glu Arg Ile Ser Val
 100 105 110

Ser Ala Ala Ser Lys Leu Leu Ser Asn Met Met Cys Gln Tyr Arg Gly
 115 120 125

Met Gly Leu Ser Met Gly Ser Met Ile Cys Gly Trp Asp Lys Lys Gly
130 135 140

Pro Gly Leu Tyr Tyr Val Asp Glu His Gly Thr Arg Leu Ser Gly Asn
145 150 155 160

Met Phe Ser Thr Gly Ser Gly Asn Thr Tyr Ala Tyr Gly Val Met Asp
165 170 175

Ser Gly Tyr Arg Pro Asn Leu Ser Pro Glu Glu Ala Tyr Asp Leu Gly
180 185 190

Arg Arg Ala Ile Ala Tyr Ala Thr His Arg Asp Ser Tyr Ser Gly Gly
195 200 205

Val Val Asn Met Tyr His Ile Asp Thr Thr Met Val Gly Glu Ser Lys
210 215 220

Val Asp Val Asp Leu Cys Pro Pro Glu Ala Gln Ser Gly
225 230 235

<210> 153

<211> 297

<212> PRT

<213> Homo sapien

<220>

<221> MISC_FEATURE

<222> (297)..(297)

<223> X=any amino acid

<400> 153

Leu Ser Phe Ser Arg Lys Arg Gln Gly Asp Val Glu Lys Ser Leu Val
1 5 10 15

Pro Ser Pro Ser Ile Cys Gly Phe Arg Phe His Phe Leu Leu Arg Glu
20 25 30

Arg Thr Asp Leu Trp Val Leu Gly Gly His Gly Ala Thr Arg Cys Met
35 40 45

Arg Ser Pro Arg Gly Gln Arg Pro Glu Ser Ala Leu Pro Val Ala Gly
50 55 60

Ser Gly Arg Arg Ser Asp Pro Gly His Tyr Ser Phe Ser Met Arg Ser
65 70 75 80

Pro Glu Leu Ala Leu Pro Arg Gly Met Gln Pro Thr Glu Phe Phe Gln
 85 90 95

Ser Leu Gly Gly Asp Gly Glu Arg Asn Val Gln Ile Glu Met Ala His
 100 105 110

Gly Thr Thr Thr Leu Ala Phe Lys Phe Gln His Gly Val Ile Ala Ala
 115 120 125

Val Asp Ser Arg Ala Ser Ala Gly Ser Tyr Ile Ser Ala Leu Arg Val
 130 135 140

Asn Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr Met Ser Gly
 145 150 155 160

Cys Ala Ala Asp Cys Gln Tyr Trp Glu Arg Leu Leu Ala Lys Glu Cys
 165 170 175

Arg Leu Tyr Tyr Leu Arg Asn Gly Glu Arg Ile Ser Val Ser Ala Ala
 180 185 190

Ser Lys Leu Leu Ser Asn Met Met Cys Gln Tyr Arg Gly Met Gly Leu
 195 200 205

Ser Met Gly Ser Met Ile Cys Gly Trp Asp Lys Lys Gly Pro Gly Leu
 210 215 220

Tyr Tyr Val Asp Glu His Gly Thr Arg Leu Ser Gly Asn Met Phe Ser
 225 230 235 240

Thr Gly Ser Gly Asn Thr Tyr Ala Tyr Gly Val Met Asp Ser Gly Tyr
 245 250 255

Arg Pro Asn Leu Ser Pro Glu Glu Ala Tyr Asp Leu Gly Arg Arg Ala
 260 265 270

Ile Ala Tyr Ala Thr His Arg Asp Ser Tyr Ser Gly Gly Val Val Asn
 275 280 285

Met Tyr His Ile Glu Arg Asp Gly Xaa
 290 295

<210> 154
 <211> 260
 <212> PRT

<213> Homo sapien

<400> 154

Met Asp Ser Ser Leu Pro Asn Ala Gln His Asp Val Gln Gly Leu Ser
 1 5 10 15

Pro Gln Glu Asn Leu Ser Pro Pro Ser Phe Pro Thr Ser Ser His Pro
 20 25 30

Gln Val Cys Gln Lys Ser Gly Glu Ile Ser Leu Leu Lys Gln Gln Leu
 35 40 45

Lys Glu Ser Gln Ala Glu Leu Val Gln Lys Gly Ser Glu Leu Val Ala
 50 55 60

Leu Arg Val Ala Leu Arg Glu Ala Arg Ala Thr Leu Arg Val Ser Glu
 65 70 75 80

Gly Arg Ala Arg Gly Leu Gln Glu Ala Ala Arg Ala Arg Glu Leu Glu
 85 90 95

Leu Glu Ala Cys Ser Gln Glu Leu Gln Arg His Arg Gln Glu Ala Glu
 100 105 110

Gln Leu Arg Glu Lys Ala Gly Gln Leu Asp Ala Glu Ala Ala Gly Leu
 115 120 125

Arg Glu Pro Pro Val Pro Pro Ala Thr Ala Asp Pro Phe Leu Leu Ala
 130 135 140

Glu Ser Asp Glu Ala Lys Val Gln Arg Ala Ala Ala Gly Val Gly Gly
 145 150 155 160

Ser Leu Arg Ala Gln Val Glu Arg Leu Arg Val Glu Leu Gln Arg Glu
 165 170 175

Arg Arg Arg Gly Glu Glu Gln Arg Asp Ser Phe Glu Gly Glu Arg Leu
 180 185 190

Ala Trp Gln Ala Glu Lys Glu Gln Val Ile Arg Tyr Gln Lys Gln Leu
 195 200 205

Gln His Asn Tyr Ile Gln Met Tyr Arg Arg Asn Arg Gln Leu Glu Gln
 210 215 220

Glu Leu Gln Gln Leu Ser Leu Glu Leu Glu Ala Arg Glu Leu Ala Asp

225					230					235					240
Leu	Gly	Leu	Ala	Glu	Gln	Ala	Pro	Cys	Ile	Cys	Leu	Glu	Glu	Ile	Thr
				245					250					255	
Ala	Thr	Glu	Ile												
			260												
<210>	155														
<211>	249														
<212>	PRT														
<213>	Homo sapien														
<400>	155														
Cys	Ala	Gly	Pro	Val	Pro	Pro	Gly	Glu	Pro	Val	Ser	Pro	Ser	Phe	Pro
1				5					10					15	
Thr	Ser	Ser	His	Pro	Gln	Val	Cys	Gln	Lys	Ser	Gly	Glu	Ile	Ser	Leu
			20					25					30		
Leu	Lys	Gln	Gln	Leu	Lys	Glu	Ser	Gln	Ala	Glu	Leu	Val	Gln	Lys	Gly
		35					40					45			
Ser	Glu	Leu	Val	Ala	Leu	Arg	Val	Ala	Leu	Arg	Glu	Ala	Arg	Ala	Thr
	50					55					60				
Leu	Arg	Val	Ser	Glu	Gly	Arg	Ala	Arg	Gly	Leu	Gln	Glu	Ala	Ala	Arg
65					70					75					80
Ala	Arg	Glu	Leu	Glu	Leu	Glu	Ala	Cys	Ser	Gln	Glu	Leu	Gln	Arg	His
				85					90					95	
Arg	Gln	Glu	Ala	Glu	Gln	Leu	Arg	Glu	Lys	Ala	Gly	Gln	Leu	Asp	Ala
			100					105					110		
Glu	Ala	Ala	Gly	Leu	Arg	Glu	Pro	Pro	Val	Pro	Pro	Ala	Thr	Ala	Asp
		115					120					125			
Pro	Phe	Leu	Leu	Ala	Glu	Ser	Asp	Glu	Ala	Lys	Val	Gln	Arg	Ala	Ala
	130					135					140				
Ala	Gly	Val	Gly	Gly	Ser	Leu	Arg	Ala	Gln	Val	Glu	Arg	Leu	Arg	Val
145					150					155					160
Glu	Leu	Gln	Arg	Glu	Arg	Arg	Arg	Gly	Glu	Glu	Gln	Arg	Asp	Ser	Phe
				165					170					175	

Glu Gly Glu Arg Leu Ala Trp Gln Ala Glu Lys Glu Gln Val Ile Arg
 180 185 190

Tyr Gln Lys Gln Leu Gln His Asn Tyr Ile Gln Met Tyr Arg Arg Asn
 195 200 205

Arg Gln Leu Glu Gln Glu Leu Gln Gln Leu Ser Leu Glu Leu Glu Ala
 210 215 220

Arg Glu Leu Ala Asp Leu Gly Leu Ala Glu Gln Ala Pro Cys Ile Cys
 225 230 235 240

Leu Glu Glu Ile Thr Ala Thr Glu Ile
 245

<210> 156

<211> 132

<212> PRT

<213> Homo sapien

<400> 156

Met Arg Gly Ser His Leu Pro Gln Pro Gln Thr His Phe Ser Lys Trp
 1 5 10 15

Ser Leu His Leu Pro Leu Leu Leu Phe Arg Ala Pro Arg Ala Gly Ala
 20 25 30

Gly Leu Ala Gly Pro Gly Phe Pro Asp Ser Trp Leu Trp Leu Pro Gly
 35 40 45

Cys Val Ala Leu Arg Ala Arg Leu Cys Gly Thr Leu Asp Leu Trp Ala
 50 55 60

Leu Gly Ser Val Gly Leu Gly Gly Pro Gly Ser Leu Gly Pro Ala Gly
 65 70 75 80

Cys Pro Leu Val Gly Leu Thr Leu Gly Pro Leu Arg Val Phe Val Ser
 85 90 95

Phe Gly Ser Leu Ser Phe Ser Glu Pro Val Ser Phe Leu Gln Phe Ser
 100 105 110

Leu Ser Pro Cys Ser Leu Lys Trp Gly Asn Ala Thr Glu Val Pro Ala
 115 120 125

Pro Leu Ala Pro

130

<210> 157
 <211> 225
 <212> PRT
 <213> Homo sapien

<220>
 <221> MISC_FEATURE
 <222> (23)..(23)
 <223> X=any amino acid

<400> 157

Ala Trp Ser Ser Ala Ala Glu Val Arg Gly Ala Gly Ser Gly Arg Arg
 1 5 10 15

Pro Gly Glu Pro Pro Thr Xaa Ala Arg Trp Asn Pro Ala Gly Gly Thr
 20 25 30

Ala Phe Pro Ser Arg Pro His Phe Leu Glu Gly Gly Leu Asp Ser Gly
 35 40 45

Glu Trp Val Arg Gly Ser Trp Leu Pro Ala Ala Glu Trp Glu Leu Val
 50 55 60

Ile Ala Asp Leu Thr Pro Leu Asp Trp Ser Leu Glu Phe Gly Trp Glu
 65 70 75 80

Gly Asp Phe Pro Gln Leu Phe Arg Ser Val Ser Gly Pro Glu Pro Ala
 85 90 95

Pro Ala Leu Cys Ser Pro Gln Pro Thr Lys Arg Gly Val Leu Leu Gly
 100 105 110

Gln Ser Asp Cys Ser Gly Ser Ala Gly Glu Asn Glu Gly Phe Pro Ser
 115 120 125

Pro Thr Ala Thr Asn Ala Phe Leu Lys Met Glu Pro Pro Leu Ala Pro
 130 135 140

Pro Ser Leu Ser Gly Ser Lys Ser Gly Ser Arg Pro Gly Trp Ala Trp
 145 150 155 160

Leu Ser Arg Leu Leu Ala Leu Ala Pro Trp Met Cys Gly Ser Gln Gly
 165 170 175

Pro Ala Leu Trp His Phe Gly Leu Met Gly Pro Arg Leu Arg Gly Val

10/538002

180

185

190

JC17 Rec'd PCT/PTO 03 JUN 2005

Gly Gly Pro Trp Leu Thr Gly Ser Arg Trp Leu Ser Pro Cys Arg Pro
 195 200 205

Asp Pro Arg Ala Ser Pro Ser Leu Cys Leu Phe Trp Val Pro Val Phe
 210 215 220

Leu
 225

<210> 158
 <211> 451
 <212> PRT
 <213> Homo sapien

<400> 158

Ala Ser Ala Thr Met Ala Ile Val Gln Thr Leu Pro Val Pro Leu Glu
 1 5 10 15

Pro Ala Pro Glu Ala Ala Thr Ala Pro Gln Ala Pro Val Met Gly Ser
 20 25 30

Val Ser Ser Leu Ile Ser Gly Arg Pro Cys Pro Gly Gly Pro Ala Pro
 35 40 45

Pro Arg His His Gly Pro Pro Gly Pro Thr Phe Phe Arg Gln Gln Asp
 50 55 60

Gly Leu Leu Arg Gly Gly Tyr Glu Ala Gln Glu Pro Leu Cys Pro Ala
 65 70 75 80

Val Pro Pro Arg Lys Ala Val Pro Val Thr Ser Phe Thr Tyr Ile Asn
 85 90 95

Glu Asp Phe Arg Thr Glu Ser Pro Pro Ser Pro Ser Ser Asp Val Glu
 100 105 110

Asp Ala Arg Glu Gln Arg Ala His Asn Ala His Leu Arg Gly Pro Pro
 115 120 125

Pro Lys Leu Ile Pro Val Ser Gly Lys Leu Glu Lys Asn Met Glu Lys
 130 135 140

Ile Leu Ile Arg Pro Thr Ala Phe Lys Pro Val Leu Pro Lys Pro Arg
 145 150 155 160

260/383

Gly Ala Pro Ser Leu Pro Ser Phe Met Gly Pro Arg Ala Thr Gly Leu
165 170 175

Ser Gly Ser Gln Gly Ser Leu Thr Gln Leu Phe Gly Gly Pro Ala Ser
180 185 190

Ser Ser Ser Ser Ser Ser Ser Ser Ala Ala Asp Lys Pro Leu Ala
195 200 205

Phe Ser Gly Trp Ala Ser Gly Cys Pro Ser Gly Thr Leu Ser Asp Ser
210 215 220

Gly Arg Asn Ser Leu Ser Ser Leu Pro Thr Tyr Ser Thr Gly Gly Ala
225 230 235 240

Glu Pro Thr Thr Ser Ser Pro Gly Gly His Leu Pro Ser His Gly Ser
245 250 255

Gly Arg Gly Ala Leu Pro Gly Pro Ala Arg Gly Val Pro Thr Gly Pro
260 265 270

Ser His Ser Asp Ser Gly Arg Ser Ser Ser Ser Lys Ser Thr Gly Ser
275 280 285

Leu Gly Gly Arg Val Ala Gly Gly Leu Leu Gly Ser Gly Thr Arg Ala
290 295 300

Ser Pro Asp Ser Ser Ser Cys Gly Glu Arg Ser Pro Pro Pro Pro Pro
305 310 315 320

Pro Pro Pro Ser Asp Glu Ala Leu Leu His Cys Val Leu Glu Gly Lys
325 330 335

Leu Arg Asp Arg Glu Ala Glu Leu Gln Gln Leu Arg Asp Ser Leu Asp
340 345 350

Glu Asn Glu Ala Thr Met Cys Gln Ala Tyr Glu Glu Arg Gln Arg His
355 360 365

Trp Gln Arg Glu Arg Glu Ala Leu Arg Glu Asp Cys Ala Ala Gln Ala
370 375 380

Gln Arg Ala Gln Arg Ala Gln Gln Leu Leu Gln Leu Gln Val Phe Gln
385 390 395 400

261/383

Leu Gln Gln Glu Lys Arg Gln Leu Gln Asp Asp Phe Ala Gln Leu Leu
 405 410 415

Gln Glu Arg Glu Gln Leu Glu Arg Arg Cys Ala Thr Leu Glu Arg Glu
 420 425 430

Arg Arg Arg Gly Glu Glu Gln Arg Asp Ser Phe Glu Gly Glu Arg Asp
 435 440 445

His Cys Tyr
 450

<210> 159
 <211> 1193
 <212> PRT
 <213> Homo sapien

<400> 159

Met Glu Arg His Gln Pro Arg Leu His His Pro Ala Gln Gly Ser Ala
 1 5 10 15

Ala Gly Thr Pro Tyr Pro Ser Ser Ala Ser Leu Arg Gly Cys Arg Glu
 20 25 30

Ser Lys Met Pro Arg Arg Lys Gly Pro Gln His Pro Pro Pro Ser
 35 40 45

Gly Pro Glu Glu Pro Gly Glu Lys Arg Pro Lys Phe His Leu Asn Ile
 50 55 60

Arg Thr Leu Thr Asp Asp Met Leu Asp Lys Phe Ala Ser Ile Arg Ile
 65 70 75 80

Pro Gly Ser Lys Lys Glu Arg Pro Pro Leu Pro Asn Leu Lys Thr Ala
 85 90 95

Phe Ala Ser Ser Asp Cys Ser Ala Ala Pro Leu Glu Met Met Glu Asn
 100 105 110

Phe Pro Lys Pro Leu Ser Glu Asn Glu Leu Leu Glu Leu Phe Glu Lys
 115 120 125

Met Met Glu Asp Met Asn Leu Asn Glu Asp Lys Lys Ala Pro Leu Arg
 130 135 140

Glu Lys Asp Phe Ser Ile Lys Lys Glu Met Val Met Gln Tyr Ile Asn
 145 150 155 160

Thr Ala Ser Lys Thr Gly Ser Leu Lys Arg Ser Arg Gln Ile Ser Pro
165 170 175

Gln Glu Phe Ile His Glu Leu Lys Met Gly Ser Ala Asp Glu Arg Leu
180 185 190

Val Thr Cys Leu Glu Ser Leu Arg Val Ser Leu Thr Ser Asn Pro Val
195 200 205

Ser Trp Val Glu Ser Phe Gly His Glu Gly Leu Gly Leu Leu Leu Asp
210 215 220

Ile Leu Glu Lys Leu Ile Ser Gly Lys Ile Gln Glu Lys Val Val Lys
225 230 235 240

Lys Asn Gln His Lys Val Ile Gln Cys Leu Lys Ala Leu Met Asn Thr
245 250 255

Gln Tyr Gly Leu Glu Arg Ile Met Ser Glu Glu Arg Ser Leu Ser Leu
260 265 270

Leu Ala Lys Ala Val Asp Pro Arg His Pro Asn Met Met Thr Asp Val
275 280 285

Val Lys Leu Leu Ser Ala Val Cys Ile Val Gly Glu Glu Ser Ile Leu
290 295 300

Glu Glu Val Leu Glu Ala Leu Thr Ser Ala Gly Glu Glu Lys Lys Ile
305 310 315 320

Asp Arg Phe Phe Cys Ile Val Glu Gly Leu Arg His Asn Ser Val Gln
325 330 335

Leu Gln Val Ala Cys Met Gln Leu Ile Asn Ala Leu Val Thr Ser Pro
340 345 350

Asp Asp Leu Asp Phe Arg Leu His Ile Arg Asn Glu Phe Met Arg Cys
355 360 365

Gly Leu Lys Glu Ile Leu Pro Asn Leu Lys Cys Ile Lys Asn Asp Gly
370 375 380

Leu Asp Ile Gln Leu Lys Val Phe Asp Glu His Lys Glu Glu Asp Leu
385 390 395 400

Phe Glu Leu Ser His Arg Leu Glu Asp Ile Arg Ala Glu Leu Asp Glu
 405 410 415

Ala Tyr Asp Val Tyr Asn Met Val Trp Ser Thr Val Lys Glu Thr Arg
 420 425 430

Ala Glu Gly Tyr Phe Ile Ser Ile Leu Gln His Leu Leu Leu Ile Arg
 435 440 445

Asn Asp Tyr Phe Ile Arg Gln Gln Tyr Phe Lys Leu Ile Asp Glu Cys
 450 455 460

Val Ser Gln Ile Val Leu His Arg Asp Gly Met Asp Pro Asp Phe Thr
 465 470 475 480

Tyr Arg Lys Arg Leu Asp Leu Asp Leu Thr Gln Phe Val Asp Ile Cys
 485 490 495

Ile Asp Gln Ala Lys Leu Glu Glu Phe Glu Glu Lys Ala Ser Glu Leu
 500 505 510

Tyr Lys Lys Phe Glu Lys Glu Phe Thr Asp His Gln Glu Thr Gln Ala
 515 520 525

Glu Leu Gln Lys Lys Glu Ala Lys Ile Asn Glu Leu Gln Ala Glu Leu
 530 535 540

Gln Ala Phe Lys Ser Gln Phe Gly Ala Leu Pro Ala Asp Cys Asn Ile
 545 550 555 560

Pro Leu Pro Pro Ser Lys Glu Gly Gly Thr Gly His Ser Ala Leu Pro
 565 570 575

Pro Pro Pro Pro Leu Pro Ser Gly Gly Gly Val Pro Pro Pro Pro Pro
 580 585 590

Pro Pro Pro Pro Pro Pro Leu Pro Gly Met Arg Met Pro Phe Ser Gly
 595 600 605

Pro Val Pro Pro Pro Pro Pro Leu Gly Phe Leu Gly Gly Gln Asn Ser
 610 615 620

Pro Pro Leu Pro Ile Leu Pro Phe Gly Leu Lys Pro Lys Lys Glu Phe
 625 630 635 640

Lys Pro Glu Ile Ser Met Arg Arg Leu Asn Trp Leu Lys Ile Arg Pro
645 650 655

His Glu Met Thr Glu Asn Cys Phe Trp Ile Lys Val Asn Glu Asn Lys
660 665 670

Tyr Glu Asn Val Asp Leu Leu Cys Lys Leu Glu Asn Thr Phe Cys Cys
675 680 685

Gln Gln Lys Glu Arg Arg Glu Glu Glu Asp Ile Glu Glu Lys Lys Ser
690 695 700

Ile Lys Lys Lys Ile Lys Glu Leu Lys Phe Leu Asp Ser Lys Ile Ala
705 710 715 720

Gln Asn Leu Ser Ile Phe Leu Ser Ser Phe Arg Val Pro Tyr Glu Glu
725 730 735

Ile Arg Met Met Ile Leu Glu Val Asp Glu Thr Arg Leu Ala Glu Ser
740 745 750

Met Ile Gln Asn Leu Ile Lys His Leu Pro Asp Gln Glu Gln Leu Asn
755 760 765

Ser Leu Ser Gln Phe Lys Ser Glu Tyr Ser Asn Leu Cys Glu Pro Glu
770 775 780

Gln Phe Val Val Val Met Ser Asn Val Lys Arg Leu Arg Pro Arg Leu
785 790 795 800

Ser Ala Ile Leu Phe Lys Leu Gln Phe Glu Glu Gln Val Asn Asn Ile
805 810 815

Lys Pro Asp Ile Met Ala Val Ser Thr Ala Cys Glu Glu Ile Lys Lys
820 825 830

Ser Lys Ser Phe Ser Lys Leu Leu Glu Leu Val Leu Leu Met Gly Asn
835 840 845

Tyr Met Asn Ala Gly Ser Arg Asn Ala Gln Thr Phe Gly Phe Asn Leu
850 855 860

Ser Ser Leu Cys Lys Leu Lys Asp Thr Lys Ser Ala Asp Gln Lys Thr
865 870 875 880

Thr Leu Leu His Phe Leu Val Glu Ile Cys Glu Glu Lys Tyr Pro Asp

885	890	895
Ile Leu Asn Phe Val Asp Asp Leu Glu Pro Leu Asp Lys Ala Ser Lys 900 905 910		
Val Ser Val Glu Thr Leu Glu Lys Asn Leu Arg Gln Met Gly Arg Gln 915 920 925		
Leu Gln Gln Leu Glu Lys Glu Leu Glu Thr Phe Pro Pro Pro Glu Asp 930 935 940		
Leu His Asp Lys Phe Val Thr Lys Met Ser Arg Phe Val Ile Ser Ala 945 950 955 960		
Lys Glu Gln Tyr Glu Thr Leu Ser Lys Leu His Glu Asn Met Glu Lys 965 970 975		
Leu Tyr Gln Ser Ile Ile Gly Tyr Tyr Ala Ile Asp Val Lys Lys Val 980 985 990		
Ser Val Glu Asp Phe Leu Thr Asp Leu Asn Asn Phe Arg Thr Thr Phe 995 1000 1005		
Met Gln Ala Ile Lys Glu Asn Ile Lys Lys Arg Glu Ala Glu Glu 1010 1015 1020		
Lys Glu Lys Arg Val Arg Ile Ala Lys Glu Leu Ala Glu Arg Glu 1025 1030 1035		
Arg Leu Glu Arg Gln Gln Lys Lys Lys Arg Leu Leu Glu Met Lys 1040 1045 1050		
Thr Glu Gly Asp Glu Thr Gly Val Met Asp Asn Leu Leu Glu Ala 1055 1060 1065		
Leu Gln Ser Gly Ala Ala Phe Arg Asp Arg Arg Lys Arg Thr Pro 1070 1075 1080		
Met Pro Lys Asp Val Arg Gln Ser Leu Ser Pro Met Ser Gln Arg 1085 1090 1095		
Pro Val Leu Lys Val Cys Asn His Glu Asn Gln Lys Val Gln Leu 1100 1105 1110		
Thr Glu Gly Ser Arg Ser His Tyr Asn Ile Asn Cys Asn Ser Thr 1115 1120 1125		

Arg Thr Pro Val Ala Lys Glu Leu Asn Tyr Asn Leu Asp Thr His
 1130 1135 1140

Thr Ser Thr Gly Arg Ile Lys Ala Ala Glu Lys Lys Glu Ala Cys
 1145 1150 1155

Asn Val Glu Ser Asn Arg Lys Lys Glu Thr Glu Leu Leu Gly Ser
 1160 1165 1170

Phe Ser Lys Asn Glu Ser Val Pro Glu Val Glu Ala Leu Leu Ala
 1175 1180 1185

Arg Leu Arg Ala Leu
 1190

<210> 160
 <211> 650
 <212> PRT
 <213> Homo sapien

<400> 160

Met Ser Leu Ala Asp Glu Leu Leu Ala Asp Leu Glu Glu Ala Ala Glu
 1 5 10 15

Glu Glu Glu Gly Gly Ser Tyr Gly Glu Glu Glu Glu Glu Pro Ala Ile
 20 25 30

Glu Asp Val Gln Glu Glu Thr Gln Leu Asp Leu Ser Gly Asp Ser Val
 35 40 45

Lys Thr Ile Ala Lys Leu Trp Asp Ser Lys Met Phe Ala Glu Ile Met
 50 55 60

Met Lys Ile Glu Glu Tyr Ile Ser Lys Gln Ala Lys Ala Ser Glu Val
 65 70 75 80

Met Gly Pro Val Glu Ala Ala Pro Glu Tyr Arg Val Ile Val Asp Ala
 85 90 95

Asn Asn Leu Thr Val Glu Ile Glu Asn Glu Leu Asn Ile Ile His Lys
 100 105 110

Phe Ile Arg Asp Lys Tyr Ser Lys Arg Phe Pro Glu Leu Glu Ser Leu
 115 120 125

Val Pro Asn Ala Leu Asp Tyr Ile Arg Thr Val Lys Glu Leu Gly Asn
 130 135 140
 Ser Leu Asp Lys Cys Lys Asn Asn Glu Asn Leu Gln Gln Ile Leu Thr
 145 150 155 160
 Asn Ala Thr Ile Met Val Val Ser Val Thr Ala Ser Thr Thr Gln Gly
 165 170 175
 Gln Gln Leu Ser Glu Glu Glu Leu Glu Arg Leu Glu Glu Ala Cys Asp
 180 185 190
 Met Ala Leu Glu Leu Asn Ala Ser Lys His Arg Ile Tyr Glu Tyr Val
 195 200 205
 Glu Ser Arg Met Ser Phe Ile Ala Pro Asn Leu Ser Ile Ile Ile Gly
 210 215 220
 Ala Ser Thr Ala Ala Lys Ile Met Gly Val Ala Gly Gly Leu Thr Asn
 225 230 235 240
 Leu Ser Lys Met Pro Ala Cys Asn Ile Met Leu Leu Gly Ala Gln Arg
 245 250 255
 Lys Thr Leu Ser Gly Phe Ser Ser Thr Ser Val Leu Pro His Thr Gly
 260 265 270
 Tyr Ile Tyr His Ser Asp Ile Val Gln Ser Leu Pro Pro Asp Leu Arg
 275 280 285
 Arg Lys Ala Ala Arg Leu Val Ala Ala Lys Cys Thr Leu Ala Ala Arg
 290 295 300
 Val Asp Ser Phe His Glu Ser Thr Glu Gly Lys Val Gly Tyr Glu Leu
 305 310 315 320
 Lys Asp Glu Ile Glu Arg Lys Phe Asp Lys Trp Gln Glu Pro Pro Pro
 325 330 335
 Val Lys Gln Val Lys Pro Leu Pro Ala Pro Leu Asp Gly Gln Arg Lys
 340 345 350
 Lys Arg Gly Gly Arg Ser Val Arg Gly Pro Gly Gly Pro Val Gly Met
 355 360 365
 Gly Val Met Glu Gly Arg Ser Arg Arg Pro Pro Pro Ser Arg Leu Pro

370	375	380
Gly Ala Ala His Pro Pro Val Pro Val Pro Gln Asp Glu Gly Ala Ala		
385	390	395 400
Gly Ala Asp Gly Asp Pro Glu Ala Gly Gln Pro Tyr Glu Leu Arg Arg		
	405	410 415
Gly Gln Thr Pro Arg Ala Pro Ser Ser Thr Pro Gln Pro Ala Ser Arg		
	420	425 430
His Arg Pro Leu Pro Pro Ala Thr Ala Pro Pro Leu Val Leu Trp Pro		
	435	440 445
Trp Leu Met Ser Arg Ala Leu Pro Gln Pro Pro Pro Pro Arg Pro Leu		
	450	455 460
Phe Ser Phe Pro Ser Ile Gln Pro Gln Ser Asp Pro Arg Gly Pro Trp		
465	470	475 480
Ser Leu Cys Leu Arg Cys Leu Glu Pro Pro Arg Leu Pro Ile Ala Pro		
	485	490 495
Gly Ser Leu Ala Gly Ser Ser Leu Pro Arg Gly Ser Leu Val Pro Cys		
	500	505 510
Cys Thr Ala Ala Pro Ser Leu Gly Pro Ala Ser Leu Leu Cys Tyr Pro		
	515	520 525
Ser Val Ile Pro Leu Val Leu Gln Asp Arg Thr Gln Arg Pro Pro His		
	530	535 540
Pro Ile Lys Pro Val Leu Val Pro Asp Ile Pro Arg Pro Thr Arg Ile		
545	550	555 560
Glu Glu Asp Ala Tyr Gln Glu Asp Leu Gly Phe Ser Leu Gly His Leu		
	565	570 575
Gly Lys Ser Gly Ser Gly Arg Val Arg Gln Thr Gln Val Asn Glu Ala		
	580	585 590
Thr Lys Ala Arg Ile Ser Lys Thr Leu Gln Arg Thr Leu Gln Lys Gln		
	595	600 605
Ser Val Val Tyr Gly Gly Lys Ser Thr Ile Arg Asp Arg Ser Ser Gly		
610	615	620

Thr Ala Ser Ser Val Ala Phe Thr Pro Leu Gln Gly Pro Gly Asp Cys
625 630 635 640

Glu Pro Thr Gly Gly Arg Glu Glu Gly Gly
645 650

<210> 161
<211> 369
<212> PRT
<213> Homo sapien

<400> 161

Lys Gln Trp Cys Ala Glu Arg Arg Gly Leu Gly Met Ser Leu Ala Asp
1 5 10 15

Glu Leu Leu Ala Asp Leu Glu Glu Ala Ala Glu Glu Glu Glu Gly Gly
20 25 30

Ser Tyr Gly Glu Glu Glu Glu Glu Pro Ala Ile Glu Asp Val Gln Glu
35 40 45

Glu Thr Gln Leu Asp Leu Ser Gly Asp Ser Val Lys Thr Ile Ala Lys
50 55 60

Leu Trp Asp Ser Lys Met Phe Ala Glu Ile Met Met Lys Ile Glu Glu
65 70 75 80

Tyr Ile Ser Lys Gln Ala Lys Ala Ser Glu Val Met Gly Pro Val Glu
85 90 95

Ala Ala Pro Glu Tyr Arg Val Ile Val Asp Ala Asn Asn Leu Thr Val
100 105 110

Glu Ile Glu Asn Glu Leu Asn Ile Ile His Lys Phe Ile Arg Asp Lys
115 120 125

Tyr Ser Lys Arg Phe Pro Glu Leu Glu Ser Leu Val Pro Asn Ala Leu
130 135 140

Asp Tyr Ile Arg Thr Val Lys Glu Leu Gly Asn Ser Leu Asp Lys Cys
145 150 155 160

Lys Asn Asn Glu Asn Leu Gln Gln Ile Leu Thr Asn Ala Thr Ile Met
165 170 175

270/383

Val Val Ser Val Thr Ala Ser Thr Thr Gln Gly Gln Gln Leu Ser Glu
180 185 190

Glu Glu Leu Glu Arg Leu Glu Glu Ala Cys Asp Met Ala Leu Glu Leu
195 200 205

Asn Ala Ser Lys His Arg Ile Tyr Glu Tyr Val Glu Ser Arg Met Ser
210 215 220

Phe Ile Ala Pro Asn Leu Ser Ile Ile Ile Gly Ala Ser Thr Ala Ala
225 230 235 240

Lys Ile Met Gly Val Ala Gly Gly Leu Thr Asn Leu Ser Lys Met Pro
245 250 255

Ala Cys Asn Ile Met Leu Leu Gly Ala Gln Arg Lys Thr Leu Ser Gly
260 265 270

Phe Ser Ser Thr Ser Val Leu Pro His Thr Gly Tyr Ile Tyr His Ser
275 280 285

Asp Ile Val Gln Ser Leu Pro Pro Asp Leu Arg Arg Lys Ala Ala Arg
290 295 300

Leu Val Ala Ala Lys Cys Thr Leu Ala Ala Arg Val Asp Ser Phe His
305 310 315 320

Glu Ser Thr Glu Gly Lys Val Gly Tyr Glu Leu Lys Asp Glu Ile Glu
325 330 335

Arg Lys Phe Asp Lys Trp Gln Glu Pro Pro Pro Val Lys Gln Val Lys
340 345 350

Pro Leu Pro Ala Pro Leu Asp Gly Gln Arg Lys Lys Arg Gly Gly Arg
355 360 365

Arg

<210> 162
<211> 164
<212> PRT
<213> Homo sapien

<400> 162

Arg Arg Pro Tyr Ala Gly Thr Arg Leu Pro Val Gly Ser Pro Gly Leu
1 5 10 15

Phe Leu Asn Ala Ala Ala Ala Thr Pro Arg Thr Pro Ser Val Thr Gly
 20 25 30

Ala Thr Glu Thr Val Thr Pro Ser Glu Ala Pro Val Leu Ala Ala Glu
 35 40 45

Pro Glu Ala Asp Lys Gly Thr Val Leu Ala Leu Thr Glu Asn Asn Phe
 50 55 60

Asp Asp Thr Ile Ala Glu Gly Ile Thr Phe Ile Lys Phe Tyr Ala Pro
 65 70 75 80

Trp Cys Gly His Cys Lys Thr Leu Ala Pro Thr Trp Glu Glu Leu Ser
 85 90 95

Lys Lys Glu Phe Pro Gly Leu Ala Gly Val Lys Ile Ala Glu Val Asp
 100 105 110

Cys Thr Ala Glu Arg Asn Ile Cys Ser Lys Tyr Ser Val Arg Gly Tyr
 115 120 125

Pro Thr Leu Leu Leu Phe Arg Gly Gly Lys Lys Val Ser Glu His Ser
 130 135 140

Gly Gly Arg Asp Leu Asp Ser Leu His Arg Phe Val Leu Ser Gln Ala
 145 150 155 160

Lys Asp Glu Leu

<210> 163

<211> 31

<212> PRT

<213> Homo sapien

<400> 163

Thr Asp Gln His Ser Ile Glu Ser Thr Val Thr Leu Arg Ser Glu Glu
 1 5 10 15

Arg Gln Tyr Cys His Lys Ala Thr Phe Pro Glu Leu Val Gly Arg
 20 25 30

<210> 164

<211> 110

<212> PRT

<213> Homo sapien

<400> 164

Pro Leu Cys Ile Gln His Ser Ser Pro Thr Ser His Thr Gln Gly Asp
 1 5 10 15

Val Asp Thr Trp Pro Lys Val Thr Gly Gly Arg Asn Leu Arg Asn Lys
 20 25 30

Thr Thr Tyr Thr Val Cys Leu Arg Gln Lys Ile Thr Ala Ala Ser Arg
 35 40 45

Pro Ala Ser Ala Leu Lys Glu Ile Phe Ile Asn His Val Trp Phe Thr
 50 55 60

Asp Asn Ser Phe Phe Lys Lys Thr Gln Pro Pro Arg Glu Ala Gln Leu
 65 70 75 80

Ser Arg Val Leu Tyr Thr Gln Leu Gln Leu Cys Ile Thr Ser Leu Val
 85 90 95

Phe Gln Glu Asn Gln Ser Gly Thr Ile Cys Leu Phe Thr Leu
 100 105 110

<210> 165

<211> 39

<212> PRT

<213> Homo sapien

<400> 165

Met Val Thr Leu Glu Phe Pro Tyr Glu Arg Arg Asp Val Lys Thr Lys
 1 5 10 15

Asp Arg Cys Gln Trp Ala Ala Leu Ala Leu Val Cys Thr Ala Val Ala
 20 25 30

Ala Val Asp Ala Ser Val Leu
 35

<210> 166

<211> 110

<212> PRT

<213> Homo sapien

<400> 166

Pro Leu Cys Ile Gln His Ser Ser Pro Thr Ser His Thr Gln Gly Asp
 1 5 10 15

273/383

Val Asp Thr Trp Pro Lys Val Thr Gly Gly Arg Asn Leu Arg Asn Lys
20 25 30

Thr Thr Tyr Thr Val Cys Leu Arg Gln Lys Ile Thr Ala Ala Ser Arg
35 40 45

Pro Ala Ser Ala Leu Lys Glu Ile Phe Ile Asn His Val Trp Phe Thr
50 55 60

Asp Asn Ser Phe Phe Lys Lys Thr Gln Pro Pro Arg Glu Ala Gln Leu
65 70 75 80

Ser Arg Val Leu Tyr Thr Gln Leu Gln Leu Cys Ile Thr Ser Leu Val
85 90 95

Phe Gln Glu Asn Gln Ser Gly Thr Ile Cys Leu Phe Thr Leu
100 105 110

<210> 167

<211> 140

<212> PRT

<213> Homo sapien

<400> 167

Met Val Gly Arg Arg Ala Leu Ile Val Leu Ala His Ser Glu Arg Thr
1 5 10 15

Ser Phe Asn Tyr Ala Met Lys Glu Ala Ala Ala Ala Ala Leu Lys Lys
20 25 30

Lys Gly Trp Glu Val Val Glu Ser Asp Leu Tyr Ala Met Asn Phe Asn
35 40 45

Pro Ile Ile Ser Arg Lys Asp Ile Thr Gly Lys Leu Lys Asp Pro Ala
50 55 60

Asn Phe Gln Tyr Pro Ala Glu Ser Val Leu Ala Tyr Lys Glu Gly His
65 70 75 80

Leu Ser Pro Asp Ile Val Ala Glu Gln Lys Lys Leu Glu Ala Ala Asp
85 90 95

Leu Val Ile Phe Gln Val Trp Gly Asp Ile Gly Arg Gly Val Arg Asp
100 105 110

Ile Cys Val Leu Ile Val Leu Asp Met Tyr Leu Ile Ser Tyr Glu Ile
115 120 125

Leu Asn Ser Tyr Pro Leu Tyr Cys Ile Leu Cys Lys
 130 135 140

<210> 168
 <211> 73
 <212> PRT
 <213> Homo sapien

<400> 168

Phe Glu Ser Val Pro Cys Lys Gly Glu Tyr Glu Thr Cys Asn Ser Asp
 1 5 10 15

Asn Leu Asn His Ala Val Leu Ala Val Gly Tyr Gly Ile Gln Lys Gly
 20 25 30

Asn Lys His Trp Ile Ile Lys Asn Ser Trp Gly Glu Asn Trp Gly Asn
 35 40 45

Lys Gly Tyr Ile Leu Met Ala Arg Asn Lys Asn Asn Ala Cys Gly Ile
 50 55 60

Ala Asn Leu Ala Ser Phe Pro Lys Met
 65 70

<210> 169
 <211> 72
 <212> PRT
 <213> Homo sapien

<400> 169

Ser Ser Arg Tyr Pro Gln Gly Glu Tyr Glu Thr Cys Asn Ser Asp Asn
 1 5 10 15

Leu Asn His Ala Val Leu Ala Val Gly Tyr Gly Ile Gln Lys Gly Asn
 20 25 30

Lys His Trp Ile Ile Lys Asn Ser Trp Gly Glu Asn Trp Gly Asn Lys
 35 40 45

Gly Tyr Ile Leu Met Ala Arg Asn Lys Asn Asn Ala Cys Gly Ile Ala
 50 55 60

Asn Leu Ala Ser Phe Pro Lys Met
 65 70

<210> 170

<211> 321

<212> PRT

<213> Homo sapien .

<400> 170

Phe Val Ser Leu Cys Ser Gly Ser Ser Ser Cys Arg Ser Leu Leu Phe
 1 5 10 15

Phe Phe Arg Phe Val Leu Ile Arg Trp Ser Phe Pro Leu Leu Ser Ser
 20 25 30

Ser Phe Ser Ser Ser Leu Phe Val Val Leu Phe Arg Arg Cys Gly Leu
 35 40 45

Val Arg Phe Ser Arg Ser Val Leu Ala Ser Val Leu Leu Ala Leu Leu
 50 55 60

Leu Leu Ser Ser Cys Val Arg Phe Pro Val Ala Cys Leu Ser Phe Ser
 65 70 75 80

Leu Leu Leu Val Ile Cys Phe Ser Leu Phe Leu Leu Phe Leu Ser Pro
 85 90 95

Val Ser Pro Ser Phe Leu Val Ser Ser Ser Pro Phe Leu Leu Phe Ala
 100 105 110

Cys Ala Cys Leu Ala Arg Ser Val Phe Phe Cys Leu Cys Phe Cys Arg
 115 120 125

Val Arg Leu Ser Leu Val Phe Phe Gly Leu Leu Phe Leu Phe Ser Pro
 130 135 140

Leu Arg Ser Leu Leu Phe Ser Val Leu Arg Ala Ser Val Pro Phe Val
 145 150 155 160

Phe Phe Val Phe Phe Ala Ser Phe Arg Ser Leu Arg Ser Ser Ser Ser
 165 170 175

Val Pro Leu Leu Ser Ser Phe Leu Pro Leu Ser Pro Phe Leu Leu Leu
 180 185 190

Trp Leu Pro Ser Leu Ala Val Leu Pro Leu Arg Leu Pro Leu Leu Pro
 195 200 205

Ser Val Val Ser Arg Cys Cys Ser Cys Val Leu Leu Cys Val Leu Val
 210 215 220

Leu Phe Trp Phe Leu Val Gly Gly Cys Val Val Cys Ala Leu Cys Val
 225 230 235 240

Leu Phe Val Val Phe Val Arg Ser Trp Cys Thr Ala Glu Lys Ser His
 245 250 255

His Gln Arg Thr Ser Phe Asn Arg Leu Ile Val Gly Ala Ser Pro Glu
 260 265 270

Gly Leu Arg Ala Gly Arg Ser Gly Gly Cys Ser Arg Leu Leu Phe Phe
 275 280 285

Ala Pro Trp Ala Leu Ser Lys Arg Ser Arg Tyr Leu Ala Leu Glu Gly
 290 295 300

Thr Leu Ala Pro Pro Phe Phe Phe Cys Met Ser Thr Phe Ala Phe Ile
 305 310 315 320

Glu

<210> 171

<211> 320

<212> PRT

<213> Homo sapien

<400> 171

Arg Leu Ala Leu Phe Trp Phe Phe Leu Val Ser Val Val Ile Val Leu
 1 5 10 15

Leu Pro Leu Arg Ser His Ser Leu Val Leu Ser Leu Ala Leu Phe Leu
 20 25 30

Leu Phe Leu Leu Pro Leu Arg Gly Ser Leu Pro Ala Leu Trp Ser Cys
 35 40 45

Ser Phe Leu Ser Val Cys Pro Gly Phe Arg Leu Val Gly Ser Ser Pro
 50 55 60

Ser Val Phe Leu Arg Pro Val Ser Cys Cys Leu Ser Val Phe Leu Ala
 65 70 75 80

Ser Ala Arg His Leu Phe Leu Leu Val Leu Ala Phe Ser Leu Ser Gly
 85 90 95

Leu Ala Phe Phe Pro Cys Leu Leu Leu Pro Phe Ser Ser Leu Cys Val

277/383

100					105					110					
Cys	Leu	Ser	Arg	Ser	Leu	Cys	Val	Leu	Leu	Ser	Leu	Leu	Leu	Ser	Cys
	115						120					125			
Pro	Leu	Val	Ser	Cys	Leu	Leu	Arg	Leu	Ala	Phe	Ser	Leu	Leu	Ser	Ser
	130						135				140				
Pro	Phe	Ala	Ala	Val	Phe	Cys	Ser	Pro	Cys	Leu	Cys	Pro	Phe	Cys	Leu
	145					150				155					160
Leu	Arg	Leu	Leu	Arg	Phe	Leu	Pro	Phe	Pro	Pro	Leu	Leu	Phe	Leu	Arg
				165					170					175	
Ser	Ser	Pro	Leu	Val	Val	Pro	Pro	Ala	Leu	Pro	Phe	Arg	Cys	Cys	Ser
			180					185					190		
Gly	Phe	Pro	Arg	Trp	Pro	Ser	Ser	Leu	Phe	Ala	Ser	Leu	Ser	Phe	Pro
	195						200					205			
Leu	Ser	Phe	Leu	Val	Val	Val	Leu	Val	Cys	Cys	Cys	Val	Cys	Ser	Cys
	210					215					220				
Cys	Ser	Gly	Ser	Trp	Leu	Val	Val	Val	Trp	Cys	Val	Arg	Cys	Val	Cys
	225				230					235					240
Cys	Leu	Leu	Cys	Leu	Cys	Ala	Arg	Gly	Val	Leu	Leu	Arg	Ser	His	Thr
			245						250					255	
Thr	Ser	Val	Arg	Arg	Leu	Thr	Gly	Tyr	Arg	Gly	Arg	Ile	Pro	Arg	Gly
			260					265					270		
Ser	Pro	Ser	Arg	Ala	Val	Arg	Arg	Leu	Phe	Pro	Pro	Ser	Phe	Phe	Cys
		275					280					285			
Ser	Leu	Gly	Pro	Val	Gln	Thr	Val	Pro	Tyr	Leu	Ala	Leu	Glu	Gly	Thr
	290					295					300				
Leu	Ala	Pro	Pro	Phe	Phe	Phe	Cys	Met	Ser	Thr	Phe	Ala	Phe	Ile	Glu
	305				310					315					320

<210> 172

<211> 320

<212> PRT

<213> Homo sapien

<400> 172

Arg Leu Ala Leu Phe Trp Phe Phe Leu Val Ser Val Val Ile Val Leu
 1 5 10 15

Leu Pro Leu Arg Ser His Ser Leu Val Leu Ser Leu Ala Leu Phe Leu
 20 25 30

Leu Phe Leu Leu Pro Leu Arg Gly Ser Leu Pro Ala Leu Trp Ser Cys
 35 40 45

Ser Phe Leu Ser Val Cys Pro Gly Phe Arg Leu Val Gly Ser Ser Pro
 50 55 60

Ser Val Phe Leu Arg Pro Val Ser Cys Cys Leu Ser Val Phe Leu Ala
 65 70 75 80

Ser Ala Arg His Leu Phe Leu Leu Val Leu Ala Phe Ser Leu Ser Gly
 85 90 95

Leu Ala Phe Phe Pro Cys Leu Leu Leu Pro Phe Ser Ser Leu Cys Val
 100 105 110

Cys Leu Ser Arg Ser Leu Cys Val Leu Leu Ser Leu Leu Leu Ser Cys
 115 120 125

Pro Leu Val Ser Cys Leu Leu Arg Leu Ala Phe Ser Leu Leu Ser Ser
 130 135 140

Pro Phe Ala Ala Val Phe Cys Ser Pro Cys Leu Cys Pro Phe Cys Leu
 145 150 155 160

Leu Arg Leu Leu Arg Phe Leu Pro Phe Pro Pro Leu Leu Phe Leu Arg
 165 170 175

Ser Ser Pro Leu Val Val Pro Pro Ala Leu Pro Phe Arg Cys Cys Ser
 180 185 190

Gly Phe Pro Arg Trp Pro Ser Ser Leu Phe Ala Ser Leu Ser Phe Pro
 195 200 205

Leu Ser Phe Leu Val Val Val Leu Val Cys Cys Cys Val Cys Ser Cys
 210 215 220

Cys Ser Gly Ser Trp Leu Val Val Val Trp Cys Val Arg Cys Val Cys
 225 230 235 240

Thr Ser Val Arg Arg Leu Thr Gly Tyr Arg Gly Arg Ile Pro Arg Gly
260 265 270

Ser Pro Ser Arg Ala Val Arg Arg Leu Phe Pro Pro Ser Phe Phe Cys
275 280 285

Ser Leu Gly Pro Val Gln Thr Val Pro Tyr Leu Ala Leu Glu Gly Thr
290 295 300

Leu Ala Pro Pro Phe Phe Phe Cys Met Ser Thr Phe Ala Phe Ile Glu
305 310 315 320

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<210> 173
<211> 684
<212> PRT
<213> Homo sapien
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<400> 173

Met Glu Glu Asn Leu Ile Ser Met Arg Glu Asp His Ser Phe His Val
1 5 10 15

Arg Tyr Arg Met Glu Ala Ser Cys Leu Glu Leu Ala Leu Glu Gly Glu
20 25 30

Arg Leu Cys Lys Ser Gly Asp Cys Arg Ala Gly Val Ser Phe Phe Glu
35 40 45

Ala Ala Val Gln Val Gly Thr Glu Asp Leu Lys Thr Leu Ser Ala Ile
50 55 60

Tyr Ser Gln Leu Gly Asn Ala Tyr Phe Tyr Leu His Asp Tyr Ala Lys
65 70 75 80

Ala Leu Glu Tyr His His His Asp Leu Thr Leu Ala Arg Thr Ile Gly
85 90 95

Asp Gln Leu Gly Glu Ala Lys Ala Ser Gly Asn Leu Gly Asn Thr Leu
100 105 110

Lys Val Leu Gly Asn Phe Asp Glu Ala Ile Val Cys Cys Gln Arg His
115 120 125

Leu Asp Ile Ser Arg Glu Leu Asn Asp Lys Val Gly Glu Ala Arg Ala
130 135 140

Leu Tyr Asn Leu Gly Asn Val Tyr His Ala Lys Gly Lys Ser Phe Gly
145 150 155 160

Cys Pro Gly Pro Gln Asp Val Gly Glu Phe Pro Glu Glu Val Arg Asp
165 170 175

Ala Leu Gln Ala Ala Val Asp Phe Tyr Glu Glu Asn Leu Ser Leu Val
180 185 190

Thr Ala Leu Gly Asp Arg Ala Ala Gln Gly Arg Ala Phe Gly Asn Leu
195 200 205

Gly Asn Thr His Tyr Leu Leu Gly Asn Phe Arg Asp Ala Val Ile Ala
210 215 220

His Glu Gln Arg Leu Leu Ile Ala Lys Glu Phe Gly Asp Lys Ala Ala
225 230 235 240

Glu Arg Arg Ala Tyr Ser Asn Leu Gly Asn Ala Tyr Ile Phe Leu Gly
245 250 255

Glu Phe Glu Thr Ala Ser Glu Tyr Tyr Lys Lys Thr Leu Leu Leu Ala
260 265 270

Arg Gln Leu Lys Asp Arg Ala Val Glu Ala Gln Ser Cys Tyr Ser Leu
275 280 285

Gly Asn Thr Tyr Thr Leu Leu Gln Asp Tyr Glu Lys Ala Ile Asp Tyr
290 295 300

His Leu Lys His Leu Ala Ile Ala Gln Glu Leu Asn Asp Arg Ile Gly
305 310 315 320

Glu Gly Arg Ala Cys Trp Ser Leu Gly Asn Ala Tyr Thr Ala Leu Gly
325 330 335

Asn His Asp Gln Ala Met His Phe Ala Glu Lys His Leu Glu Ile Ser
340 345 350

Arg Glu Val Gly Asp Lys Ser Gly Glu Leu Thr Ala Arg Leu Asn Leu
355 360 365

Ser Asp Leu Gln Met Val Leu Gly Leu Ser Tyr Ser Thr Asn Asn Ser
370 375 380

Ile Met Ser Glu Asn Thr Glu Ile Asp Ser Ser Leu Asn Gly Val Arg
385 390 395 400

Pro Lys Leu Gly Arg Arg His Ser Met Glu Asn Met Glu Leu Met Lys
405 410 415

Leu Thr Pro Glu Lys Val Gln Asn Trp Asn Ser Glu Ile Leu Ala Lys
420 425 430

Gln Lys Pro Leu Ile Ala Lys Pro Ser Ala Lys Leu Leu Phe Val Asn
435 440 445

Arg Leu Lys Gly Lys Lys Tyr Lys Thr Asn Ser Ser Thr Lys Val Leu
450 455 460

Gln Asp Ala Ser Asn Ser Ile Asp His Arg Ile Pro Asn Ser Gln Arg
465 470 475 480

Lys Ile Ser Ala Asp Thr Ile Gly Asp Glu Gly Phe Phe Asp Leu Leu
485 490 495

Ser Arg Phe Gln Ser Asn Arg Met Asp Asp Gln Arg Cys Cys Leu Gln
500 505 510

Glu Lys Asn Cys His Thr Ala Ser Thr Thr Thr Ser Ser Thr Pro Pro
515 520 525

Lys Met Met Leu Lys Thr Ser Ser Val Pro Val Val Ser Pro Asn Thr
530 535 540

Asp Glu Phe Leu Asp Leu Leu Ala Ser Ser Gln Ser Arg Arg Leu Asp
545 550 555 560

Asp Gln Arg Ala Ser Phe Ser Asn Leu Pro Gly Leu Arg Leu Thr Gln
565 570 575

Asn Ser Gln Ser Val Leu Ser His Leu Met Thr Asn Asp Asn Lys Glu
580 585 590

Ala Asp Glu Asp Phe Phe Asp Ile Leu Val Lys Cys Gln Gly Ser Arg
595 600 605

Leu Asp Asp Gln Arg Cys Ala Pro Pro Pro Ala Thr Thr Lys Gly Pro
610 615 620

Thr Val Pro Asp Glu Asp Phe Phe Ser Leu Ile Leu Arg Ser Gln Gly
625 630 635 640

Lys Arg Met Asp Glu Gln Arg Val Leu Leu Gln Arg Asp Gln Asn Arg
645 650 655

Asp Thr Asp Phe Gly Leu Lys Asp Phe Leu Gln Asn Asn Ala Leu Leu
660 665 670

Glu Phe Lys Asn Ser Gly Lys Lys Ser Ala Asp His
675 680

<210> 174

<211> 499

<212> PRT

<213> Homo sapien

<400> 174

Met Ser Gly His Ser Pro Thr Arg Gly Ala Met Gln Val Ala Met Asn
1 5 10 15

Gly Lys Ala Arg Lys Glu Ala Val Gln Thr Ala Ala Lys Glu Leu Leu
20 25 30

Lys Phe Val Asn Arg Ser Pro Ser Pro Phe His Ala Val Ala Glu Cys
35 40 45

Arg Asn Arg Leu Leu Gln Ala Gly Phe Ser Glu Leu Lys Glu Thr Glu
50 55 60

Lys Trp Asn Ile Lys Pro Glu Ser Lys Tyr Phe Met Thr Arg Asn Ser
65 70 75 80

Ser Thr Ile Ile Ala Phe Ala Val Gly Gly Gln Tyr Val Pro Gly Asn
85 90 95

Gly Phe Ser Leu Ile Gly Ala His Thr Asp Ser Pro Cys Leu Arg Val
100 105 110

Lys Arg Arg Ser Arg Arg Ser Gln Val Gly Phe Gln Gln Val Gly Val
115 120 125

Glu Thr Tyr Gly Gly Gly Ile Trp Ser Thr Trp Phe Asp Arg Asp Leu
130 135 140

Thr Leu Ala Gly Arg Val Ile Val Lys Cys Pro Thr Ser Gly Arg Leu
145 150 155 160

Glu Gln Gln Leu Val His Val Glu Arg Pro Ile Leu Arg Ile Pro His
165 170 175

Leu Ala Ile His Leu Gln Arg Asn Ile Asn Glu Asn Phe Gly Pro Asn
180 185 190

Thr Glu Met His Leu Val Pro Ile Leu Ala Thr Ala Ile Gln Glu Glu
195 200 205

Leu Glu Lys Gly Thr Pro Glu Pro Gly Pro Leu Asn Ala Val Asp Glu
210 215 220

Arg His His Ser Val Leu Met Ser Leu Leu Cys Ala His Leu Gly Leu
225 230 235 240

Ser Pro Lys Asp Ile Val Glu Met Glu Leu Cys Leu Ala Asp Thr Gln
245 250 255

Pro Ala Val Leu Gly Gly Ala Tyr Asp Glu Phe Ile Phe Ala Pro Arg
260 265 270

Leu Asp Asn Leu His Ser Cys Phe Cys Ala Leu Gln Ala Leu Ile Asp
275 280 285

Ser Cys Ala Gly Pro Gly Ser Leu Ala Thr Glu Pro His Val Arg Met
290 295 300

Val Thr Leu Tyr Asp Asn Glu Glu Val Gly Ser Glu Ser Ala Gln Gly
305 310 315 320

Ala Gln Ser Leu Leu Thr Glu Leu Val Leu Arg Arg Ile Ser Ala Ser
325 330 335

Cys Gln His Pro Thr Ala Phe Glu Glu Ala Ile Pro Lys Ser Phe Met
340 345 350

Ile Ser Ala Asp Met Ala His Ala Val His Pro Asn Tyr Leu Asp Lys
355 360 365

His Glu Glu Asn His Arg Pro Leu Phe His Lys Gly Pro Val Ile Lys
370 375 380

Val Ala Lys Ala Pro Thr Cys Arg Pro Tyr Gly Leu Leu Gln Pro Phe
385 390 395 400

Gly Asp Ala Ile Lys Thr Leu His Gln Arg Ala Leu Lys Pro Ala Asn
 405 410 415

Leu Pro Ser Thr Phe Lys Ser Thr Ala Asp Leu Ala Phe Asn Ile Val
 420 425 430

Leu Leu Leu Lys Pro Pro Ser Ile Ala Glu Pro Arg Val Asn Tyr Thr
 435 440 445

Lys Val Tyr Leu Leu Arg Pro Leu Arg Ala Gly Thr His Pro Cys Gln
 450 455 460

Gly Gly Thr Ala Ala Val Ala Gly Asp Ala Pro His Ser Ser Pro Ile
 465 470 475 480

Leu Ser Ala Thr Arg Ala Ala Gln Lys His Lys Gln Gln Gly Ala Arg
 485 490 495

Arg Arg Met

<210> 175

<211> 407

<212> PRT

<213> Homo sapien

<400> 175

Gly Ala Gly Gln Ala Ala Arg Trp Gly Arg Ala Glu Pro Gly Gly Gln
 1 5 10 15

Met Ser Gly His Ser Pro Thr Arg Gly Ala Met Gln Val Ala Met Asn
 20 25 30

Gly Lys Ala Arg Lys Glu Ala Val Gln Thr Ala Ala Lys Glu Leu Leu
 35 40 45

Lys Phe Val Asn Arg Ser Pro Ser Pro Phe His Ala Val Ala Glu Cys
 50 55 60

Arg Asn Arg Leu Leu Gln Ala Gly Phe Ser Glu Leu Lys Glu Thr Glu
 65 70 75 80

Lys Trp Asn Ile Lys Pro Glu Ser Lys Tyr Phe Met Thr Arg Asn Ser
 85 90 95

Ser Thr Ile Ile Ala Phe Ala Val Gly Gly Gln Tyr Val Pro Gly Asn

100	105	110
Gly Phe Ser Leu Ile Gly Ala His Thr Asp Ser Pro Cys Leu Arg Val 115 120 125		
Lys Arg Arg Ser Arg Arg Ser Gln Val Gly Phe Gln Gln Val Gly Val 130 135 140		
Glu Thr Tyr Gly Gly Gly Ile Trp Ser Thr Trp Phe Asp Arg Asp Leu 145 150 155 160		
Thr Leu Ala Gly Arg Val Ile Val Lys Cys Pro Thr Ser Gly Arg Leu 165 170 175		
Glu Gln Gln Leu Val His Val Glu Arg Pro Ile Leu Arg Ile Pro His 180 185 190		
Leu Ala Ile His Leu Gln Arg Asn Ile Asn Glu Asn Phe Gly Pro Asn 195 200 205		
Thr Glu Met His Leu Val Pro Ile Leu Ala Thr Ala Ile Gln Glu Glu 210 215 220		
Leu Glu Lys Gly Thr Pro Glu Pro Gly Pro Leu Asn Ala Val Asp Glu 225 230 235 240		
Arg His His Ser Val Leu Met Ser Leu Leu Cys Ala His Leu Gly Leu 245 250 255		
Ser Pro Lys Asp Ile Val Glu Met Glu Leu Cys Leu Ala Asp Thr Gln 260 265 270		
Pro Ala Val Leu Gly Gly Ala Tyr Asp Glu Phe Ile Phe Ala Pro Arg 275 280 285		
Leu Asp Asn Leu His Ser Cys Phe Cys Ala Leu Gln Ala Leu Ile Asp 290 295 300		
Ser Cys Ala Gly Pro Gly Ser Leu Ala Thr Glu Pro His Val Arg Met 305 310 315 320		
Val Thr Leu Tyr Asp Asn Glu Glu Val Gly Ser Glu Ser Ala Gln Gly 325 330 335		
Ala Gln Ser Leu Leu Thr Glu Leu Val Leu Arg Arg Ile Ser Ala Ser 340 345 350		

Cys Gln His Pro Thr Ala Phe Glu Glu Ala Ile Pro Lys Ser Phe Met
355 360 365

Ile Ser Ala Asp Met Ala His Ala Val His Pro Asn Tyr Leu Asp Lys
370 375 380

His Glu Glu Asn His Arg Pro Leu Phe His Lys Gly Pro Val Ile Lys
385 390 395 400

Val Ala Lys Ala Pro Thr Leu
405

<210> 176
<211> 31
<212> PRT
<213> Homo sapien

<400> 176

Met His Leu Ile Thr Asp Asp Glu Ala Pro Tyr Arg Thr Pro Pro Pro
1 5 10 15

Ser Asn Ala His Val Gln Arg Ser Ile Asn Ala Leu Ile Asp Tyr
20 25 30

<210> 177
<211> 69
<212> PRT
<213> Homo sapien

<400> 177

Gly Thr Ala Asn Cys Asn Pro Val Pro Ala Ser Val Asn Glu Val Ile
1 5 10 15

Phe Ile Phe Pro Ser Ile His Met Phe Ile Tyr Tyr Leu Tyr Gly Cys
20 25 30

Phe Pro Thr Lys Trp Gln Ser Trp Ala Val Ala Ile Asp Thr Ile Trp
35 40 45

Ala Ala Lys Pro Lys Ile Phe Ser Ile Trp Pro Phe Thr Glu Lys Val
50 55 60

Cys Leu Pro Leu Ser
65

<210> 178

<211> 89
<212> PRT
<213> Homo sapien

<400> 178

Thr Ser Thr Ala Gln Cys Ala Gly Ile Arg Leu Ser Ser Gly Ala Arg
1 5 10 15

Ala Gly Thr Val Asn Asn Asp Glu Gly Glu Trp Ser Gly Pro Pro Pro
20 25 30

Glu Cys Arg Gly Lys Ser Leu Thr Ser Lys Val Pro Pro Thr Val Gln
35 40 45

Lys Pro Thr Thr Val Asn Val Pro Thr Thr Glu Val Ser Pro Thr Ser
50 55 60

Gln Lys Thr Thr Thr Lys Thr Thr Thr Pro Asn Ala Gln Ala Thr Arg
65 70 75 80

Ser Thr Ser Ala Ala Thr Thr Leu Ser
85

<210> 179
<211> 86
<212> PRT
<213> Homo sapien

<400> 179

Tyr Gly Ala Val Cys Gly Ile Arg Phe Arg Ala Ala Pro Gly Ser Thr
1 5 10 15

Val Asn Asn Asp Glu Gly Glu Trp Ser Gly Pro Pro Pro Glu Cys Arg
20 25 30

Gly Lys Ser Leu Thr Ser Lys Val Pro Pro Thr Val Gln Lys Pro Thr
35 40 45

Thr Val Asn Val Pro Thr Thr Glu Val Ser Pro Thr Ser Gln Lys Thr
50 55 60

Thr Thr Lys Thr Thr Thr Pro Asn Ala Gln Ala Thr Arg Ser Thr Ser
65 70 75 80

Ala Ala Thr Thr Leu Ser
85

<210> 180
 <211> 404
 <212> PRT
 <213> Homo sapien

<400> 180

Met Leu Lys Thr Ala Ser Ala Ala Leu Thr Trp Gly Leu Gly Pro Asp
 1 5 10 15

Pro Ala Trp Ser His Pro Ala Gln Lys Thr Gly Pro Pro Val Pro Val
 20 25 30

Thr His Cys Ser Tyr Gly Ala Arg Gly Phe Trp Cys Trp Gly Pro Pro
 35 40 45

Cys Arg Trp Gly Arg Arg Arg Ser Arg Ser Cys Arg Glu Asp Gln Lys
 50 55 60

Pro Val Met Asp Asp Gln Arg Asp Leu Ile Ser Asn Asn Glu Gln Leu
 65 70 75 80

Pro Met Leu Gly Arg Arg Pro Gly Ala Pro Glu Ser Lys Cys Ser Arg
 85 90 95

Gly Ala Leu Tyr Thr Gly Phe Ser Ile Leu Val Thr Leu Leu Leu Ala
 100 105 110

Gly Gln Ala Thr Thr Ala Tyr Phe Leu Tyr Gln Gln Gln Gly Arg Leu
 115 120 125

Asp Lys Leu Thr Val Thr Ser Gln Asn Leu Gln Leu Glu Asn Leu Arg
 130 135 140

Met Lys Leu Pro Lys Pro Pro Lys Pro Val Ser Lys Met Arg Met Ala
 145 150 155 160

Thr Pro Leu Leu Met Gln Ala Leu Pro Met Gly Ala Leu Pro Gln Gly
 165 170 175

Pro Met Gln Asn Ala Thr Lys Tyr Gly Asn Met Thr Glu Asp His Val
 180 185 190

Met His Leu Leu Gln Asn Ala Asp Pro Leu Lys Val Tyr Pro Pro Leu
 195 200 205

Lys Gly Ser Phe Pro Glu Asn Leu Arg His Leu Lys Asn Thr Met Glu
 210 215 220

Thr Ile Asp Trp Lys Val Phe Glu Ser Trp Met His His Trp Leu Leu
225 230 235 240

Phe Glu Met Ser Arg His Ser Leu Glu Gln Lys Pro Thr Asp Ala Pro
245 250 255

Pro Lys Val Leu Thr Lys Cys Gln Glu Glu Val Ser His Ile Pro Ala
260 265 270

Val His Pro Gly Ser Phe Arg Pro Lys Cys Asp Glu Asn Gly Asn Tyr
275 280 285

Leu Pro Leu Gln Cys Tyr Gly Ser Ile Gly Tyr Cys Trp Cys Val Phe
290 295 300

Pro Asn Gly Thr Glu Val Pro Asn Thr Arg Ser Arg Gly His His Asn
305 310 315 320

Cys Ser Gly Lys Gln Trp His Cys Ala Ser Val Arg Gly Pro Gly Arg
325 330 335

Thr Arg Lys Val Glu Gly Gln Glu Val Pro Ser Glu Ala His Gly Thr
340 345 350

Arg Thr Pro Arg Met Ala Ala Pro Gly Gly Ser Asp Val Val Met Arg
355 360 365

Pro Ala Leu Tyr Pro Ser Thr His Leu Cys Ile Pro Ile Cys Pro Phe
370 375 380

Ile Ile Ser Pro Leu Thr Cys Thr His Ile Cys Ser Leu Ile Arg Gln
385 390 395 400

Ser Phe His Leu

<210> 181
<211> 371
<212> PRT
<213> Homo sapien

<400> 181

Leu Thr Ala Val Met Val Pro Ala Ala Ser Gly Val Gly Asp Leu Arg
1 5 10 15

290/383

Ala Val Gly Gly Arg Arg Ser Arg Ser Cys Arg Glu Asp Gln Lys Pro
 20 25 30

Val Met Asp Asp Gln Arg Asp Leu Ile Ser Asn Asn Glu Gln Leu Pro
 35 40 45

Met Leu Gly Arg Arg Pro Gly Ala Pro Glu Ser Lys Cys Ser Arg Gly
 50 55 60

Ala Leu Tyr Thr Gly Phe Ser Ile Leu Val Thr Leu Leu Leu Ala Gly
 65 70 75 80

Gln Ala Thr Thr Ala Tyr Phe Leu Tyr Gln Gln Gln Gly Arg Leu Asp
 85 90 95

Lys Leu Thr Val Thr Ser Gln Asn Leu Gln Leu Glu Asn Leu Arg Met
 100 105 110

Lys Leu Pro Lys Pro Pro Lys Pro Val Ser Lys Met Arg Met Ala Thr
 115 120 125

Pro Leu Leu Met Gln Ala Leu Pro Met Gly Ala Leu Pro Gln Gly Pro
 130 135 140

Met Gln Asn Ala Thr Lys Tyr Gly Asn Met Thr Glu Asp His Val Met
 145 150 155 160

His Leu Leu Gln Asn Ala Asp Pro Leu Lys Val Tyr Pro Pro Leu Lys
 165 170 175

Gly Ser Phe Pro Glu Asn Leu Arg His Leu Lys Asn Thr Met Glu Thr
 180 185 190

Ile Asp Trp Lys Val Phe Glu Ser Trp Met His His Trp Leu Leu Phe
 195 200 205

Glu Met Ser Arg His Ser Leu Glu Gln Lys Pro Thr Asp Ala Pro Pro
 210 215 220

Lys Val Leu Thr Lys Cys Gln Glu Glu Val Ser His Ile Pro Ala Val
 225 230 235 240

His Pro Gly Ser Phe Arg Pro Lys Cys Asp Glu Asn Gly Asn Tyr Leu
 245 250 255

Pro Leu Gln Cys Tyr Gly Ser Ile Gly Tyr Cys Trp Cys Val Phe Pro

291/383

260 265 270
 Asn Gly Thr Glu Val Pro Asn Thr Arg Ser Arg Gly His His Asn Cys
 275 280 285
 Ser Gly Lys Gln Trp His Cys Ala Ser Val Arg Gly Pro Gly Arg Thr
 290 295 300
 Arg Lys Val Glu Gly Gln Glu Val Pro Ser Glu Ala His Gly Thr Arg
 305 310 315 320
 Thr Pro Arg Met Ala Ala Pro Gly Gly Ser Asp Val Val Met Arg Pro
 325 330 335
 Ala Leu Tyr Pro Ser Thr His Leu Cys Ile Pro Ile Cys Pro Phe Ile
 340 345 350
 Ile Ser Pro Leu Thr Cys Thr His Ile Cys Ser Leu Ile Arg Gln Ser
 355 360 365
 Phe His Leu
 370
 <210> 182
 <211> 102
 <212> PRT
 <213> Homo sapien
 <400> 182
 Ile Leu His Gly Pro Leu Gly Gln Gly Ser His Gly Gln Arg Leu His
 1 5 10 15
 Gln Asn Ala Asp Pro Leu Lys Val Tyr Pro Pro Leu Lys Gly Ser Phe
 20 25 30
 Pro Glu Asn Leu Arg His Leu Lys Asn Thr Met Glu Thr Ile Asp Trp
 35 40 45
 Lys Val Phe Glu Ser Trp Met His His Trp Leu Leu Phe Glu Met Ser
 50 55 60
 Arg His Ser Leu Glu Gln Lys Pro Thr Asp Ala Pro Pro Lys Glu Ser
 65 70 75 80
 Leu Glu Leu Glu Asp Pro Ser Ser Gly Leu Gly Val Thr Lys Gln Asp
 85 90 95

Leu Gly Pro Val Pro Met
100

<210> 183
<211> 102
<212> PRT
<213> Homo sapien

<400> 183

Glu Gln Gln Arg Arg Ser Ser Thr Ser Cys Gln Pro His Thr Ala Thr
1 5 10 15

Ala Phe Leu Leu Pro Ser Ala Pro Ser Pro Ser Pro Ile Ser His Pro
20 25 30

Val Pro His Pro Met Arg Pro Trp Cys Leu Ala Leu Ser Ser Pro Leu
35 40 45

Asp Lys Thr Asn Gln Val Gly Thr Ala Asp Asn Asn Ala Ala Arg Pro
50 55 60

Cys Cys Pro Ile Ser Ile Cys Gln Gln Gly Arg Glu Val Pro Gly Ser
65 70 75 80

Gly Gln Lys Leu Asp Arg Ser Pro Phe Leu Thr Ser Gln Gln Pro Pro
85 90 95

Thr Gln Gly Ser Lys Thr
100

<210> 184
<211> 273
<212> PRT
<213> Homo sapien

<400> 184

Met Glu Gly Val Leu Cys Pro Ala Gly Trp Trp Leu Arg Pro Gln Ala
1 5 10 15

Cys Ala Gln Gly Arg Trp Gln His Ser Glu Ala Thr Ser Thr Ala Glu
20 25 30

Leu Ala Val Glu Ile Val Tyr Val Val Pro Ser Val Ala Glu Ser Leu
35 40 45

Pro Ala Pro His Trp Leu Ser Thr Gln Gly Phe Gln Asn Leu Glu Lys
50 55 60

Gly Ala Val Phe Trp Ser Trp Ser Cys Gly Val Pro Cys Ala Ser Met
65 70 75 80

Gly Trp Val Cys Ala Gln Ala Ala Leu Pro Trp Lys Cys Gly Cys Gly
85 90 95

Tyr Gly Leu Gly Val Trp Asp Pro Arg Gln Pro Lys Trp Glu Gln Gly
100 105 110

Arg Pro Val Gly Lys Gly Gly Ser Gly Leu Val Gly Ser Ala Ala Pro
115 120 125

Arg Cys Pro Phe Ser Val Gln Arg Gly Ser Asp Glu Leu Phe Ser Thr
130 135 140

Cys Val Thr Asn Gly Pro Phe Ile Met Ser Ser Asn Ser Ala Ser Ala
145 150 155 160

Ala Asn Gly Asn Asp Ser Lys Lys Phe Lys Gly Asp Ser Arg Ser Ala
165 170 175

Gly Val Pro Ser Arg Val Ile His Ile Arg Lys Leu Pro Ile Asp Val
180 185 190

Thr Glu Gly Glu Val Ile Ser Leu Gly Leu Pro Phe Gly Lys Val Thr
195 200 205

Asn Leu Leu Met Leu Lys Gly Lys Asn Gln Ala Phe Ile Glu Met Asn
210 215 220

Thr Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser Val Thr
225 230 235 240

Pro Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Leu Cys Ala Leu
245 250 255

Ser Thr Ala Pro Ala Ser Cys Pro Gly Gly Ser Pro Arg Ile Pro Phe
260 265 270

Pro

<210> 185
<211> 227
<212> PRT

<213> Homo sapien

<400> 185

Glu Pro Pro Ser Pro Thr Leu Ala Glu Tyr Pro Gly Leu Pro Glu Phe
 1 5 10 15

Gly Lys Arg Ser Ser Val Leu Val Val Glu Leu Trp Gly Ala Val Arg
 20 25 30

Val His Gly Leu Gly Leu Arg Ser Gly Cys Pro Ala Val Glu Val Trp
 35 40 45

Val Trp Val Trp Val Gly Gly Leu Gly Pro Gln Ala Ala Gln Val Gly
 50 55 60

Ala Gly Pro Ala Gly Gly Glu Gly Arg Leu Trp Pro Gly Gly Lys Cys
 65 70 75 80

Ser Ser Ala Leu Ser Leu Leu Leu Gln Arg Gly Ser Asp Glu Leu Phe
 85 90 95

Ser Thr Cys Val Thr Asn Gly Pro Phe Ile Met Ser Ser Asn Ser Ala
 100 105 110

Ser Ala Ala Asn Gly Asn Asp Ser Lys Lys Phe Lys Gly Asp Ser Arg
 115 120 125

Ser Ala Gly Val Pro Ser Arg Val Ile His Ile Arg Lys Leu Pro Ile
 130 135 140

Asp Val Thr Glu Gly Glu Val Ile Ser Leu Gly Leu Pro Phe Gly Lys
 145 150 155 160

Val Thr Asn Leu Leu Met Leu Lys Gly Lys Asn Gln Ala Phe Ile Glu
 165 170 175

Met Asn Thr Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser
 180 185 190

Val Thr Pro Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Leu Cys
 195 200 205

Ala Leu Ser Thr Ala Pro Ala Ser Cys Pro Gly Gly Ser Pro Arg Ile
 210 215 220

Pro Phe Pro

225

<210> 186
 <211> 452
 <212> PRT
 <213> Homo sapien

<400> 186

Met Lys Ala Trp Phe Phe Pro Phe Ser Ile Arg Arg Leu Val Thr Phe
 1 5 10 15

Pro Lys Gly Ser Pro Arg Glu Met Thr Ser Pro Ser Val Thr Ser Met
 20 25 30

Gly Leu Phe Arg Arg Leu His Ser Val Pro Arg Gly Ser Ala Leu Cys
 35 40 45

Ala Met Asp Gly Ile Val Pro Asp Ile Ala Val Gly Thr Lys Arg Gly
 50 55 60

Ser Asp Glu Leu Phe Ser Thr Cys Val Thr Asn Gly Pro Phe Ile Met
 65 70 75 80

Ser Ser Asn Ser Ala Ser Ala Ala Asn Gly Asn Asp Ser Lys Lys Phe
 85 90 95

Lys Gly Asp Ser Arg Ser Ala Gly Val Pro Ser Arg Val Ile His Ile
 100 105 110

Arg Lys Leu Pro Ile Asp Val Thr Glu Gly Glu Val Ile Ser Leu Gly
 115 120 125

Leu Pro Phe Gly Lys Val Thr Asn Leu Leu Met Leu Lys Gly Lys Asn
 130 135 140

Gln Val Pro Glu Pro Arg Phe Ser Gly Val Leu Ile Thr Val Gln Ala
 145 150 155 160

Gly Thr Arg Arg Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile
 165 170 175

Glu Met Asn Thr Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr
 180 185 190

Ser Val Thr Pro Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser
 195 200 205

Asn His Lys Glu Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala
210 215 220

Gln Ala Ala Leu Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala
225 230 235 240

Leu Ala Ala Ser Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly
245 250 255

Gln Ser Pro Val Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val
260 265 270

Thr Leu Asp Val Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu
275 280 285

Lys Ile Ile Thr Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln
290 295 300

Tyr Ala Asp Pro Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly
305 310 315 320

Gln Asn Ile Tyr Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys
325 330 335

Leu Thr Ser Leu Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr
340 345 350

Thr Arg Pro Asp Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln
355 360 365

Thr Met Ala Ala Ala Phe Ala Ser Pro Tyr Ala Gly Ala Gly Phe Pro
370 375 380

Pro Thr Phe Ala Ile Pro Gln Ala Ala Gly Tyr Ser Asn Ala Trp Ser
385 390 395 400

Trp Phe Pro Ser Asp Cys Met Pro Thr Pro Pro Ser Gln Ala Ala Pro
405 410 415

His Pro Arg Arg Gln Pro Gly Arg Thr Gly His Ser Ser Ala Arg Ser
420 425 430

Gly Ala Leu Pro Gly Arg Gly Asp Ala Thr Ser Thr Glu Gln Ala Trp
435 440 445

Pro Gly Gln Trp
450

<210> 187
<211> 304
<212> PRT
<213> Homo sapien

<400> 187

Ala Ala Phe Leu Arg Gly Ala His Thr Val Gln Ala Gly Thr Arg Arg
1 5 10 15

Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile Glu Met Asn Thr
20 25 30

Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser Val Thr Pro
35 40 45

Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser Asn His Lys Glu
50 55 60

Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala Gln Ala Ala Leu
65 70 75 80

Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala Leu Ala Ala Ser
85 90 95

Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly Gln Ser Pro Val
100 105 110

Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val Thr Leu Asp Val
115 120 125

Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu Lys Ile Ile Thr
130 135 140

Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln Tyr Ala Asp Pro
145 150 155 160

Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly Gln Asn Ile Tyr
165 170 175

Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys Leu Thr Ser Leu
180 185 190

Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr Thr Arg Pro Asp
195 200 205

Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln Thr Met Ala Ala
 210 215 220

Ala Phe Ala Ser Pro Tyr Ala Gly Ala Gly Phe Pro Pro Thr Phe Ala
 225 230 235 240

Ile Pro Gln Ala Ala Gly Tyr Ser Asn Ala Trp Ser Trp Phe Pro Ser
 245 250 255

Asp Cys Met Pro Thr Pro Pro Ser Gln Ala Ala Pro His Pro Arg Arg
 260 265 270

Gln Pro Gly Arg Thr Gly His Ser Ser Ala Arg Ser Gly Ala Leu Pro
 275 280 285

Gly Arg Gly Asp Ala Thr Ser Thr Glu Gln Ala Trp Pro Gly Gln Trp
 290 295 300

<210> 188
 <211> 606
 <212> PRT
 <213> Homo sapien

<400> 188

Met Lys Ala Trp Phe Phe Pro Phe Ser Ile Arg Arg Leu Val Thr Phe
 1 5 10 15

Pro Lys Gly Ser Pro Arg Glu Met Thr Ser Pro Ser Val Thr Ser Met
 20 25 30

Gly Leu Phe Arg Arg Leu His Ser Val Pro Arg Gly Ser Ala Leu Cys
 35 40 45

Ala Met Asp Gly Ile Val Pro Asp Ile Ala Val Gly Thr Lys Arg Gly
 50 55 60

Ser Asp Glu Leu Phe Ser Thr Cys Val Thr Asn Gly Pro Phe Ile Met
 65 70 75 80

Ser Ser Asn Ser Ala Ser Ala Ala Asn Gly Asn Asp Ser Lys Lys Phe
 85 90 95

Lys Gly Asp Ser Arg Ser Ala Gly Val Pro Ser Arg Val Ile His Ile
 100 105 110

Arg Lys Leu Pro Ile Asp Val Thr Glu Gly Glu Val Ile Ser Leu Gly
 115 120 125

Leu Pro Phe Gly Lys Val Thr Asn Leu Leu Met Leu Lys Gly Lys Asn
 130 135 140

Gln Val Pro Glu Pro Arg Phe Ser Gly Val Leu Thr Pro Cys Arg Arg
 145 150 155 160

Gly Arg Gly Gly Pro Ser Ala His Cys Leu Pro Asn Glu Ala Phe Ile
 165 170 175

Glu Met Asn Thr Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr
 180 185 190

Ser Val Thr Pro Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser
 195 200 205

Asn His Lys Glu Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala
 210 215 220

Gln Ala Ala Leu Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala
 225 230 235 240

Leu Ala Ala Ser Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly
 245 250 255

Gln Ser Pro Val Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val
 260 265 270

Thr Leu Asp Val Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu
 275 280 285

Lys Ile Ile Thr Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln
 290 295 300

Tyr Ala Asp Pro Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly
 305 310 315 320

Gln Asn Ile Tyr Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys
 325 330 335

Leu Thr Ser Leu Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr
 340 345 350

Thr Arg Pro Asp Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln

355	360	365
Thr Met Ala Ala Ala Phe Gly Tyr Arg Gly Cys Pro Thr Arg Arg Gln		
370	375	380
Cys Ala Glu Trp Ser Ile Arg Ala Ala Gln Ser Gly Ala Pro Ala Ala		
385	390	395 400
Arg Ala Arg Pro Cys Thr Arg Val Met His Leu Leu Leu Ser Ala Arg		
	405	410 415
Pro Ala Gln His Gly Pro Val Ser Pro Thr Ser Gly Pro Arg Pro Pro		
	420	425 430
Leu Glu Gln Arg Ile Cys Pro Arg Arg Leu Cys Arg Gly Arg Pro Pro		
	435	440 445
Ala Gly Leu Gly Pro Ile Pro Gln His Ser Ala Arg Ser Leu Val Glu		
	450	455 460
Val Val Gly Ala Met Ile Ser Val Ser Phe Ile Ser Arg Cys Thr Trp		
465	470	475 480
Tyr Asn Leu Ser Leu Ser Val Cys Arg Ser Trp Phe Pro Ser His Leu		
	485	490 495
Cys His Ser Ser Ser Cys Arg Val Phe Lys Arg Leu Val Leu Val Pro		
	500	505 510
Gln Arg Leu His Ala His Thr Thr Phe Pro Gly Ser Ser Ala Ser Thr		
	515	520 525
Ala Ala Ala Trp Ala Asp Trp Ala Leu Glu Cys Gln Val Arg Gly Pro		
	530	535 540
Ser Arg Glu Arg Gly Arg His Val His Arg Ala Gly Leu Ala Arg Ala		
545	550	555 560
Val Val Gly Gln Gly Cys Gly Gly Pro Arg Val Asp Gly Ala Ser Gln		
	565	570 575
Lys Pro Leu Ile Ala Gln Ser Leu Trp Ser Gly Ser Leu Gln Ala Pro		
	580	585 590
Pro Gly Glu Arg Glu Asp Arg Gln Trp Leu Glu Gly Cys Leu		
	595	600 605

<210> 189
 <211> 227
 <212> PRT
 <213> Homo sapien

<400> 189

Ala Ala Phe Leu Arg Gly Ala His Thr Val Gln Ala Gly Thr Arg Arg
 1 5 10 15

Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile Glu Met Asn Thr
 20 25 30

Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser Val Thr Pro
 35 40 45

Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser Asn His Lys Glu
 50 55 60

Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala Gln Ala Ala Leu
 65 70 75 80

Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala Leu Ala Ala Ser
 85 90 95

Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly Gln Ser Pro Val
 100 105 110

Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val Thr Leu Asp Val
 115 120 125

Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu Lys Ile Ile Thr
 130 135 140

Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln Tyr Ala Asp Pro
 145 150 155 160

Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly Gln Asn Ile Tyr
 165 170 175

Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys Leu Thr Ser Leu
 180 185 190

Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr Thr Arg Pro Asp
 195 200 205

Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln Thr Met Ala Ala
 210 215 220

Ala Phe Gly
 225

<210> 190
 <211> 432
 <212> PRT
 <213> Homo sapien

<400> 190

Met Lys Ala Trp Phe Phe Pro Phe Ser Ile Arg Arg Leu Val Thr Phe
 1 5 10 15

Pro Lys Gly Ser Pro Arg Glu Met Thr Ser Pro Ser Val Thr Ser Met
 20 25 30

Gly Leu Phe Arg Arg Leu His Ser Val Pro Arg Gly Ser Ala Leu Cys
 35 40 45

Ala Met Asp Gly Ile Val Pro Asp Ile Ala Val Gly Thr Lys Arg Gly
 50 55 60

Ser Asp Glu Leu Phe Ser Thr Cys Val Thr Asn Gly Pro Phe Ile Met
 65 70 75 80

Ser Ser Asn Ser Ala Ser Ala Ala Asn Gly Asn Asp Ser Lys Lys Phe
 85 90 95

Lys Gly Asp Ser Arg Ser Ala Gly Val Pro Ser Arg Val Ile His Ile
 100 105 110

Arg Lys Leu Pro Ile Asp Val Thr Glu Gly Glu Val Ile Ser Leu Gly
 115 120 125

Leu Pro Phe Gly Lys Val Thr Asn Leu Leu Met Leu Lys Gly Lys Asn
 130 135 140

Gln Val Pro Glu Pro Arg Phe Ser Gly Val Leu Ile Thr Val Gln Ala
 145 150 155 160

Gly Thr Arg Arg Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile
 165 170 175

Glu Met Asn Thr Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr
 180 185 190

Ser Val Thr Pro Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser
195 200 205

Asn His Lys Glu Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala
210 215 220

Gln Ala Ala Leu Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala
225 230 235 240

Leu Ala Ala Ser Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly
245 250 255

Gln Ser Pro Val Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val
260 265 270

Thr Leu Asp Val Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu
275 280 285

Lys Ile Ile Thr Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln
290 295 300

Tyr Ala Asp Pro Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly
305 310 315 320

Gln Asn Ile Tyr Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys
325 330 335

Leu Thr Ser Leu Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr
340 345 350

Thr Arg Pro Asp Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln
355 360 365

Thr Met Ala Ala Ala Phe Gly Leu Ser Val Pro Asn Val His Gly Ala
370 375 380

Leu Ala Pro Leu Ala Ile Pro Ser Ala Ala Ala Ala Ala Ala Ala
385 390 395 400

Gly Arg Ile Ala Ile Pro Gly Leu Ala Gly Ala Gly Asn Ser Val Leu
405 410 415

Leu Val Ser Asn Leu Asn Pro Glu Ala Ser Thr Val Thr Cys Ser Ala
420 425 430

<210> 191
 <211> 284
 <212> PRT
 <213> Homo sapien

<400> 191

Ala Ala Phe Leu Arg Gly Ala His Thr Val Gln Ala Gly Thr Arg Arg
 1 5 10 15

Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile Glu Met Asn Thr
 20 25 30

Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser Val Thr Pro
 35 40 45

Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser Asn His Lys Glu
 50 55 60

Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala Gln Ala Ala Leu
 65 70 75 80

Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala Leu Ala Ala Ser
 85 90 95

Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly Gln Ser Pro Val
 100 105 110

Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val Thr Leu Asp Val
 115 120 125

Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu Lys Ile Ile Thr
 130 135 140

Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln Tyr Ala Asp Pro
 145 150 155 160

Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly Gln Asn Ile Tyr
 165 170 175

Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys Leu Thr Ser Leu
 180 185 190

Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr Thr Arg Pro Asp
 195 200 205

Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln Thr Met Ala Ala

210

215

220

Ala Phe Gly Leu Ser Val Pro Asn Val His Gly Ala Leu Ala Pro Leu
 225 230 235 240

Ala Ile Pro Ser Ala Ala Ala Ala Ala Ala Ala Gly Arg Ile Ala
 245 250 255

Ile Pro Gly Leu Ala Gly Ala Gly Asn Ser Val Leu Leu Val Ser Asn
 260 265 270

Leu Asn Pro Glu Ala Ser Thr Val Thr Cys Ser Ala
 275 280

<210> 192
 <211> 304
 <212> PRT
 <213> Homo sapien

<400> 192

Ala Ala Phe Leu Arg Gly Ala His Thr Val Gln Ala Gly Thr Arg Arg
 1 5 10 15

Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile Glu Met Asn Thr
 20 25 30

Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser Val Thr Pro
 35 40 45

Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser Asn His Lys Glu
 50 55 60

Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala Gln Ala Ala Leu
 65 70 75 80

Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala Leu Ala Ala Ser
 85 90 95

Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly Gln Ser Pro Val
 100 105 110

Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val Thr Leu Asp Val
 115 120 125

Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu Lys Ile Ile Thr
 130 135 140

Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln Tyr Ala Asp Pro
 145 150 155 160

Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly Gln Asn Ile Tyr
 165 170 175

Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys Leu Thr Ser Leu
 180 185 190

Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr Thr Arg Pro Asp
 195 200 205

Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln Thr Met Ala Ala
 210 215 220

Ala Phe Ala Ser Pro Tyr Ala Gly Ala Gly Phe Pro Pro Thr Phe Ala
 225 230 235 240

Ile Pro Gln Ala Ala Gly Tyr Ser Asn Ala Trp Ser Trp Phe Pro Ser
 245 250 255

Asp Cys Met Pro Thr Pro Pro Ser Gln Ala Ala Pro His Pro Arg Arg
 260 265 270

Gln Pro Gly Arg Thr Gly His Ser Ser Ala Arg Ser Gly Ala Leu Pro
 275 280 285

Gly Arg Gly Asp Ala Thr Ser Thr Glu Gln Ala Trp Pro Gly Gln Trp
 290 295 300

<210> 193

<211> 304

<212> PRT

<213> Homo sapien

<400> 193

Ala Ala Phe Leu Arg Gly Ala His Thr Val Gln Ala Gly Thr Arg Arg
 1 5 10 15

Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile Glu Met Asn Thr
 20 25 30

Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser Val Thr Pro
 35 40 45

Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser Asn His Lys Glu

307/383

50	55	60
Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala Gln Ala Ala Leu 65 70 75 80		
Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala Leu Ala Ala Ser 85 90 95		
Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly Gln Ser Pro Val 100 105 110		
Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val Thr Leu Asp Val 115 120 125		
Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu Lys Ile Ile Thr 130 135 140		
Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln Tyr Ala Asp Pro 145 150 155 160		
Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly Gln Asn Ile Tyr 165 170 175		
Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys Leu Thr Ser Leu 180 185 190		
Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr Thr Arg Pro Asp 195 200 205		
Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln Thr Met Ala Ala 210 215 220		
Ala Phe Ala Ser Pro Tyr Ala Gly Ala Gly Phe Pro Pro Thr Phe Ala 225 230 235 240		
Ile Pro Gln Ala Ala Gly Tyr Ser Asn Ala Trp Ser Trp Phe Pro Ser 245 250 255		
Asp Cys Met Pro Thr Pro Pro Ser Gln Ala Ala Pro His Pro Arg Arg 260 265 270		
Gln Pro Gly Arg Thr Gly His Ser Ser Ala Arg Ser Gly Ala Leu Pro 275 280 285		
Gly Arg Gly Asp Ala Thr Ser Thr Glu Gln Ala Trp Pro Gly Gln Trp 290 295 300		

<210> 194
 <211> 304
 <212> PRT
 <213> Homo sapien

<400> 194

Ala Ala Phe Leu Arg Gly Ala His Thr Val Gln Ala Gly Thr Arg Arg
 1 5 10 15

Ala Gln Arg Ser Leu Pro Pro Gln Gln Ala Phe Ile Glu Met Asn Thr
 20 25 30

Glu Glu Ala Ala Asn Thr Met Val Asn Tyr Tyr Thr Ser Val Thr Pro
 35 40 45

Val Leu Arg Gly Gln Pro Ile Tyr Ile Gln Phe Ser Asn His Lys Glu
 50 55 60

Leu Lys Thr Asp Ser Ser Pro Asn Gln Ala Arg Ala Gln Ala Ala Leu
 65 70 75 80

Gln Ala Val Asn Ser Val Gln Ser Gly Asn Leu Ala Leu Ala Ala Ser
 85 90 95

Ala Ala Ala Val Asp Ala Gly Met Ala Met Ala Gly Gln Ser Pro Val
 100 105 110

Leu Arg Ile Ile Val Glu Asn Leu Phe Tyr Pro Val Thr Leu Asp Val
 115 120 125

Leu His Gln Ile Phe Ser Lys Phe Gly Thr Val Leu Lys Ile Ile Thr
 130 135 140

Phe Thr Lys Asn Asn Gln Phe Gln Ala Leu Leu Gln Tyr Ala Asp Pro
 145 150 155 160

Val Ser Ala Gln His Ala Lys Leu Ser Leu Asp Gly Gln Asn Ile Tyr
 165 170 175

Asn Ala Cys Cys Thr Leu Arg Ile Asp Phe Ser Lys Leu Thr Ser Leu
 180 185 190

Asn Val Lys Tyr Asn Asn Asp Lys Ser Arg Asp Tyr Thr Arg Pro Asp
 195 200 205

Leu Pro Ser Gly Asp Ser Gln Pro Ser Leu Asp Gln Thr Met Ala Ala
 210 215 220

Ala Phe Ala Ser Pro Tyr Ala Gly Ala Gly Phe Pro Pro Thr Phe Ala
 225 230 235 240

Ile Pro Gln Ala Ala Gly Tyr Ser Asn Ala Trp Ser Trp Phe Pro Ser
 245 250 255

Asp Cys Met Pro Thr Pro Pro Ser Gln Ala Ala Pro His Pro Arg Arg
 260 265 270

Gln Pro Gly Arg Thr Gly His Ser Ser Ala Arg Ser Gly Ala Leu Pro
 275 280 285

Gly Arg Gly Asp Ala Thr Ser Thr Glu Gln Ala Trp Pro Gly Gln Trp
 290 295 300

<210> 195

<211> 315

<212> PRT

<213> Homo sapien

<400> 195

Met Arg Ser Val Gln Ala Gly Leu Ser Ser Gln Glu Ser Leu Ser Pro
 1 5 10 15

Val Leu Ser Leu Ser Pro Asp Ser Met Ser Phe Thr Thr Arg Ser Thr
 20 25 30

Phe Ser Thr Asn Tyr Arg Ser Leu Gly Ser Val Gln Ala Pro Ser Tyr
 35 40 45

Gly Ala Arg Pro Val Ser Ser Ala Ala Ser Val Tyr Ala Gly Ala Gly
 50 55 60

Gly Ser Gly Ser Arg Ile Ser Val Ser Arg Ser Thr Ser Phe Arg Gly
 65 70 75 80

Gly Met Gly Ser Gly Gly Leu Ala Thr Gly Ile Ala Gly Gly Leu Ala
 85 90 95

Gly Met Gly Gly Ile Gln Asn Glu Lys Glu Thr Met Gln Ser Leu Asn
 100 105 110

Asp Arg Leu Ala Ser Tyr Leu Asp Arg Val Arg Ser Leu Glu Thr Glu
 115 120 125

Asn Arg Arg Leu Glu Ser Lys Ile Arg Glu His Leu Glu Lys Lys Gly
 130 135 140

Pro Gln Val Arg Asp Trp Ser His Tyr Phe Lys Ile Ile Glu Asp Leu
 145 150 155 160

Arg Ala Gln Ile Phe Ala Asn Thr Val Asp Asn Ala Arg Ile Val Leu
 165 170 175

Gln Ile Asp Asn Ala Arg Leu Ala Ala Asp Asp Phe Arg Val Lys Tyr
 180 185 190

Glu Thr Glu Leu Ala Met Arg Gln Ser Val Glu Asn Asp Ile His Gly
 195 200 205

Leu Arg Lys Val Ile Asp Asp Thr Asn Ile Thr Arg Leu Gln Leu Glu
 210 215 220

Thr Glu Ile Glu Ala Leu Lys Glu Glu Leu Leu Phe Met Lys Lys Asn
 225 230 235 240

His Glu Glu Asp Arg Thr Ala Ala Thr Ser Pro Asp Ala Ser Ser Gly
 245 250 255

Leu Pro Arg Arg Gln Asn Ala Pro Asn Thr Gly Thr Gly Arg Pro Gly
 260 265 270

Asp Ser Ala Arg Asp Glu Trp Ser Arg Pro Arg Gly Glu Gly Arg Gln
 275 280 285

Asn Gly Glu Pro Arg Pro Lys Arg Ser Val Asn Glu Pro Val Glu Arg
 290 295 300

Pro Gly Ser Asp Asp Ser Gly His Gly Gly Thr
 305 310 315

<210> 196

<211> 296

<212> PRT

<213> Homo sapien

<220>

<221> MISC_FEATURE

<222> (245)..(245)

<223> X=any amino acid

<220>
 <221> MISC_FEATURE
 <222> (250)..(251)
 <223> X=any amino acid

<220>
 <221> MISC_FEATURE
 <222> (253)..(254)
 <223> X=any amino acid

<220>
 <221> MISC_FEATURE
 <222> (257)..(258)
 <223> X=any amino acid

<400> 196

His Arg Ser Val Gln Ala Gly Leu Ser Ser Gln Glu Ser Leu Ser Pro
 1 5 10 15

Val Leu Ser Leu Ser Pro Asp Ser Met Ser Phe Thr Thr Arg Ser Thr
 20 25 30

Phe Ser Thr Asn Tyr Arg Ser Leu Gly Ser Val Gln Ala Pro Ser Tyr
 35 40 45

Gly Ala Arg Pro Val Ser Ser Ala Ala Ser Val Tyr Ala Gly Ala Gly
 50 55 60

Gly Ser Gly Ser Arg Ile Ser Val Ser Arg Ser Thr Ser Phe Arg Gly
 65 70 75 80

Gly Met Gly Ser Gly Gly Leu Ala Thr Gly Ile Ala Gly Gly Leu Ala
 85 90 95

Gly Met Gly Gly Ile Gln Asn Glu Lys Glu Thr Met Gln Ser Leu Asn
 100 105 110

Asp Arg Leu Ala Ser Tyr Leu Asp Arg Val Arg Ser Leu Glu Thr Glu
 115 120 125

Asn Arg Arg Leu Glu Ser Lys Ile Arg Glu His Leu Glu Lys Lys Gly
 130 135 140

Pro Gln Val Arg Asp Trp Ser His Tyr Phe Lys Ile Ile Glu Asp Leu
 145 150 155 160

Arg Ala Gln Ile Phe Ala Asn Thr Val Asp Asn Ala Arg Ile Val Leu

165 170 175
 Gln Ile Asp Asn Ala Arg Leu Ala Ala Asp Asp Phe Arg Val Lys Tyr
 180 185 190
 Glu Thr Glu Leu Ala Met Arg Gln Ser Val Glu Asn Asp Ile His Gly
 195 200 205
 Leu Arg Lys Val Ile Asp Asp Thr Asn Ile Thr Arg Leu Gln Leu Glu
 210 215 220
 Thr Glu Ile Glu Ala Leu Lys Glu Glu Leu Leu Phe Met Lys Lys Asn
 225 230 235 240
 His Glu Glu Asp Xaa Thr Gly Leu Gln Xaa Xaa Met Xaa Xaa Leu Gly
 245 250 255
 Xaa Xaa Glu Glu Met Pro Pro Thr Pro Gly Leu Ala Asp Gln Ala Thr
 260 265 270
 Arg Gln Glu Thr Ser Gly Arg Asp Arg Gly Glu Lys Val Ala Arg Met
 275 280 285
 Gly Ser His Gly Pro Ser Gly Val
 290 295
 <210> 197
 <211> 267
 <212> PRT
 <213> Homo sapien
 <400> 197
 Met Ser Phe Thr Thr Arg Ser Thr Phe Ser Thr Asn Tyr Arg Ser Leu
 1 5 10 15
 Gly Ser Val Gln Ala Pro Ser Tyr Gly Ala Arg Pro Val Ser Ser Ala
 20 25 30
 Ala Ser Val Tyr Ala Gly Ala Gly Gly Ser Gly Ser Arg Ile Ser Val
 35 40 45
 Ser Arg Ser Thr Ser Phe Arg Gly Gly Met Gly Ser Gly Gly Leu Ala
 50 55 60
 Thr Gly Ile Ala Gly Gly Leu Ala Gly Met Gly Gly Ile Gln Asn Glu
 65 70 75 80

Lys Glu Thr Met Gln Ser Leu Asn Asp Arg Leu Ala Ser Tyr Leu Asp
85 90 95

Arg Val Arg Ser Leu Glu Thr Glu Asn Arg Arg Leu Glu Ser Lys Ile
100 105 110

Arg Glu His Leu Glu Lys Lys Gly Pro Gln Val Arg Asp Trp Ser His
115 120 125

Tyr Phe Lys Ile Ile Glu Asp Leu Arg Ala Gln Ile Phe Ala Asn Thr
130 135 140

Val Asp Asn Ala Arg Ile Val Leu Gln Ile Asp Asn Ala Arg Leu Ala
145 150 155 160

Ala Asp Asp Phe Arg Val Lys Tyr Glu Thr Glu Leu Ala Met Arg Gln
165 170 175

Ser Val Glu Asn Asp Ile His Gly Leu Arg Lys Val Ile Asp Asp Thr
180 185 190

Asn Ile Thr Arg Leu Gln Leu Glu Thr Glu Ile Glu Ala Leu Lys Glu
195 200 205

Glu Leu Leu Phe Met Lys Lys Asn His Glu Glu Glu Val Lys Gly Leu
210 215 220

Gln Ala Gln Ile Ala Ser Ser Gly Val Asp Arg Gly Gly Arg Cys Pro
225 230 235 240

Gln Ile Ser Gly Pro Arg Gln Asp His Gly Arg His Ser Gly Pro Asn
245 250 255

Met Thr Ser Trp Leu Gly Arg Thr Glu Arg Ser
260 265

<210> 198
<211> 454
<212> PRT
<213> Homo sapien

<400> 198

Lys Ala Ala Ser Arg Ala Asn Asn Thr Cys Cys Pro Cys Pro Cys Pro
1 5 10 15

Val Gly His Pro Val Ser Gly Gly Met Ser Phe Thr Thr Arg Ser Thr

20					25					30					
Phe	Ser	Thr	Asn	Tyr	Arg	Ser	Leu	Gly	Ser	Val	Gln	Ala	Pro	Ser	Tyr
		35					40					45			
Gly	Ala	Arg	Pro	Val	Ser	Ser	Ala	Ala	Ser	Val	Tyr	Ala	Gly	Ala	Gly
	50					55					60				
Gly	Ser	Gly	Ser	Arg	Ile	Ser	Val	Ser	Arg	Ser	Thr	Ser	Phe	Arg	Gly
65				70						75					80
Gly	Met	Gly	Ser	Gly	Gly	Leu	Ala	Thr	Gly	Ile	Ala	Gly	Gly	Leu	Ala
				85					90					95	
Gly	Met	Gly	Gly	Ile	Gln	Asn	Glu	Lys	Glu	Thr	Met	Gln	Ser	Leu	Asn
			100					105					110		
Asp	Arg	Leu	Ala	Ser	Tyr	Leu	Asp	Arg	Val	Arg	Ser	Leu	Glu	Thr	Glu
		115					120					125			
Asn	Arg	Arg	Leu	Glu	Ser	Lys	Ile	Arg	Glu	His	Leu	Glu	Lys	Lys	Gly
	130					135					140				
Pro	Gln	Val	Arg	Asp	Trp	Ser	His	Tyr	Phe	Lys	Ile	Ile	Glu	Asp	Leu
145					150					155					160
Arg	Ala	Gln	Ile	Phe	Ala	Asn	Thr	Val	Asp	Asn	Ala	Arg	Ile	Val	Leu
				165					170					175	
Gln	Ile	Asp	Asn	Ala	Arg	Leu	Ala	Ala	Asp	Asp	Phe	Arg	Val	Lys	Tyr
			180					185					190		
Glu	Thr	Glu	Leu	Ala	Met	Arg	Gln	Ser	Val	Glu	Asn	Asp	Ile	His	Gly
		195					200					205			
Leu	Arg	Lys	Val	Ile	Asp	Asp	Thr	Asn	Ile	Thr	Arg	Leu	Gln	Leu	Glu
	210					215					220				
Thr	Glu	Ile	Glu	Ala	Leu	Lys	Glu	Glu	Leu	Leu	Phe	Met	Lys	Lys	Asn
225					230					235					240
His	Glu	Glu	Glu	Val	Lys	Gly	Leu	Gln	Ala	Gln	Ile	Ala	Ser	Ser	Gly
				245					250					255	
Leu	Thr	Val	Glu	Val	Asp	Ala	Pro	Lys	Ser	Gln	Asp	Leu	Ala	Lys	Ile
			260					265					270		

Met Ala Asp Ile Arg Ala Gln Tyr Asp Glu Leu Ala Arg Lys Asn Arg
 275 280 285

Glu Glu Leu Asp Lys Tyr Trp Ser Gln Gln Ile Glu Glu Ser Thr Thr
 290 295 300

Val Val Thr Thr Gln Ser Ala Glu Val Gly Ala Ala Glu Thr Thr Leu
 305 310 315 320

Thr Glu Leu Arg Arg Thr Val Gln Ser Leu Glu Ile Asp Leu Asp Ser
 325 330 335

Met Arg Asn Leu Lys Ala Ser Leu Glu Asn Ser Leu Arg Glu Val Glu
 340 345 350

Ala Arg Tyr Ala Leu Gln Met Glu Gln Leu Asn Gly Ile Leu Leu His
 355 360 365

Leu Glu Ser Glu Leu Ala Gln Thr Arg Ala Glu Gly Gln Arg Gln Ala
 370 375 380

Gln Glu Tyr Glu Ala Leu Leu Asn Ile Lys Val Lys Leu Glu Ala Glu
 385 390 395 400

Ile Ala Thr Tyr Arg Arg Leu Leu Glu Asp Gly Glu Asp Phe Asn Leu
 405 410 415

Gly Asp Ala Leu Asp Ser Ser Asn Ser Met Gln Thr Ile Gln Lys Thr
 420 425 430

Thr Thr Arg Arg Ile Val Asp Gly Lys Val Val Ser Glu Thr Asn Asp
 435 440 445

Thr Lys Val Leu Arg His
 450

<210> 199
 <211> 104
 <212> PRT
 <213> Homo sapien

<400> 199

Met Leu Glu Thr Lys Trp Ser Leu Leu Gln Gln Gln Lys Thr Ala Arg
 1 5 10 15

Ser Asn Met Asp Asn Met Phe Glu Ser Tyr Ile Asn Asn Leu Arg Arg
 20 25 30

Gln Leu Glu Thr Leu Gly Gln Glu Lys Leu Lys Leu Glu Ala Glu Leu
 35 40 45

Gly Asn Met Gln Gly Leu Val Glu Asp Phe Lys Asn Lys Ser Glu Gln
 50 55 60

Leu Pro Pro Ser Thr Gln Leu Lys Ser Pro Cys Ser Pro Pro Pro Leu
 65 70 75 80

Gly Thr Leu Gly Leu Ser Pro His Gly Pro Leu Leu Trp Ala Val Gln
 85 90 95

Ser Tyr Leu Ile Arg Val Thr Thr
 100

<210> 200
 <211> 768
 <212> PRT
 <213> Homo sapien

<400> 200

Met Gly Gly Ala Glu Arg Gly Arg Ala Pro Ala Phe Leu Leu Arg Ser
 1 5 10 15

Ala Pro Val Ser Ala Gly Gly Gly Gly Ala Tyr Ile Thr Cys Ala Ala
 20 25 30

Pro Leu Leu Arg Glu Asp Val Ala Cys Ser Leu Ala Pro Gly Glu Ser
 35 40 45

Pro Arg Leu Pro Arg Glu Leu Gly Glu Arg Asn Trp Arg Arg Ser Thr
 50 55 60

Pro Gly Gly Ser Ala Leu Gln His Glu Pro Ile Ser Ser Arg Ser Arg
 65 70 75 80

Ser Arg Arg Pro Gly Arg Gly Ala Ala Ser Glu Asp Glu Asn Gly Asp
 85 90 95

Asp Gln Gly Phe Gln Glu Gly Glu Asp Glu Leu Gly Asp Glu Glu Glu
 100 105 110

Gly Ala Gly Asp Glu Asn Gly His Gly Glu Gln Gln Pro Gln Pro Pro
 115 120 125

317/383

Ala Thr Gln Gln Gln Gln Pro Gln Gln Gln Arg Gly Ala Ala Lys Glu
130 135 140

Ala Ala Gly Lys Ser Ser Gly Pro Thr Ser Leu Phe Ala Val Thr Val
145 150 155 160

Ala Pro Pro Gly Ala Arg Gln Gly Gln Gln Gln Ala Gly Gly Asp Gly
165 170 175

Lys Thr Glu Gln Lys Gly Gly Asp Lys Lys Arg Gly Val Lys Arg Pro
180 185 190

Arg Glu Asp His Gly Arg Gly Tyr Phe Glu Tyr Ile Glu Glu Asn Lys
195 200 205

Tyr Ser Arg Ala Lys Ser Pro Gln Pro Pro Val Glu Glu Glu Asp Glu
210 215 220

His Phe Asp Asp Thr Val Val Cys Leu Asp Thr Tyr Asn Cys Asp Leu
225 230 235 240

His Phe Lys Ile Ser Arg Asp Arg Leu Ser Ala Ser Ser Leu Thr Met
245 250 255

Glu Ser Phe Ala Phe Leu Trp Ala Gly Gly Arg Ala Ser Tyr Gly Val
260 265 270

Ser Lys Gly Lys Val Cys Phe Glu Met Lys Val Thr Glu Lys Ile Pro
275 280 285

Val Arg His Leu Tyr Thr Lys Asp Ile Asp Ile His Glu Val Arg Ile
290 295 300

Gly Trp Ser Leu Thr Thr Ser Gly Met Leu Leu Gly Glu Glu Glu Phe
305 310 315 320

Ser Tyr Gly Tyr Ser Leu Lys Gly Ile Lys Thr Cys Asn Cys Glu Thr
325 330 335

Glu Asp Tyr Gly Glu Lys Phe Asp Glu Asn Asp Val Ile Thr Cys Phe
340 345 350

Ala Asn Phe Glu Ser Asp Glu Val Glu Leu Ser Tyr Ala Lys Asn Gly
355 360 365

Gln Asp Leu Gly Val Ala Phe Lys Ile Ser Lys Glu Val Leu Ala Gly
 370 375 380

Arg Pro Leu Phe Pro His Val Leu Cys His Asn Cys Ala Val Glu Phe
 385 390 395 400

Asn Phe Gly Gln Lys Glu Lys Pro Tyr Phe Pro Ile Pro Glu Glu Tyr
 405 410 415

Thr Phe Ile Gln Asn Val Pro Leu Glu Asp Arg Val Arg Gly Pro Lys
 420 425 430

Gly Pro Glu Glu Lys Lys Asp Cys Glu Val Val Met Met Ile Gly Leu
 435 440 445

Pro Gly Ala Gly Lys Thr Thr Trp Val Thr Lys His Ala Ala Glu Asn
 450 455 460

Pro Gly Lys Tyr Asn Ile Leu Gly Thr Asn Thr Ile Met Asp Lys Met
 465 470 475 480

Met Val Ala Gly Phe Lys Lys Gln Met Ala Asp Thr Gly Lys Leu Asn
 485 490 495

Thr Leu Leu Gln Arg Ala Pro Gln Cys Leu Gly Lys Phe Ile Glu Ile
 500 505 510

Ala Ala Arg Lys Lys Arg Asn Phe Ile Leu Asp Gln Thr Asn Val Ser
 515 520 525

Ala Ala Ala Gln Arg Arg Lys Met Cys Leu Phe Ala Gly Phe Gln Arg
 530 535 540

Lys Ala Val Val Val Cys Pro Lys Asp Glu Asp Tyr Lys Gln Arg Thr
 545 550 555 560

Gln Lys Lys Ala Glu Val Glu Gly Lys Asp Leu Pro Glu His Ala Val
 565 570 575

Leu Lys Met Lys Gly Asn Phe Thr Leu Pro Glu Val Ala Glu Cys Phe
 580 585 590

Asp Glu Ile Thr Tyr Val Glu Leu Gln Lys Glu Glu Ala Gln Lys Leu
 595 600 605

Leu Glu Gln Tyr Lys Glu Glu Ser Lys Lys Ala Leu Pro Pro Glu Lys
 610 615 620

Lys Gln Asn Thr Gly Ser Lys Lys Ser Asn Lys Asn Lys Ser Gly Lys
 625 630 635 640

Asn Gln Phe Asn Arg Gly Gly Gly His Arg Gly Arg Gly Gly Phe Asn
 645 650 655

Met Arg Gly Gly Asn Phe Arg Gly Gly Ala Pro Gly Asn Arg Gly Gly
 660 665 670

Tyr Asn Arg Arg Gly Asn Met Pro Gln Arg Gly Gly Gly Gly Gly Gly
 675 680 685

Ser Gly Gly Ile Gly Tyr Pro Tyr Pro Arg Ala Pro Val Phe Pro Gly
 690 695 700

Arg Gly Ser Tyr Ser Asn Arg Gly Asn Tyr Asn Arg Gly Gly Met Pro
 705 710 715 720

Asn Arg Gly Asn Tyr Asn Gln Asn Phe Arg Gly Arg Gly Asn Asn Arg
 725 730 735

Gly Tyr Lys Asn Gln Ser Gln Gly Tyr Asn Gln Trp Gln Gln Gly Gln
 740 745 750

Phe Trp Gly Gln Lys Pro Trp Ser Gln His Tyr His Gln Gly Tyr Tyr
 755 760 765

<210> 201

<211> 793

<212> PRT

<213> Homo sapien

<400> 201

Ile Gly Ser Ala Leu Arg Gly Leu His Arg Ala Leu Gly Pro Gly Ser
 1 5 10 15

Ala Trp Gly Arg Gly Gly Lys Tyr Gly Asn Gly Arg Gly Arg Ala Arg
 20 25 30

Ala Arg Ser Gly Phe Pro Pro Ala Gln Cys Ser Arg Gln Arg Arg Gly
 35 40 45

Arg Gly Ala Tyr Ile Thr Cys Ala Ala Pro Leu Leu Arg Glu Asp Val
 50 55 60

Ala Cys Ser Leu Ala Pro Gly Glu Ser Pro Arg Leu Pro Arg Glu Leu
65 70 75 80

Gly Glu Arg Asn Trp Arg Arg Ser Thr Pro Gly Gly Ser Ala Leu Gln
85 90 95

His Glu Pro Ile Ser Ser Arg Ser Arg Ser Arg Arg Pro Gly Arg Gly
100 105 110

Ala Ala Ser Glu Asp Glu Asn Gly Asp Asp Gln Gly Phe Gln Glu Gly
115 120 125

Glu Asp Glu Leu Gly Asp Glu Glu Glu Gly Ala Gly Asp Glu Asn Gly
130 135 140

His Gly Glu Gln Gln Pro Gln Pro Pro Ala Thr Gln Gln Gln Gln Pro
145 150 155 160

Gln Gln Gln Arg Gly Ala Ala Lys Glu Ala Ala Gly Lys Ser Ser Gly
165 170 175

Pro Thr Ser Leu Phe Ala Val Thr Val Ala Pro Pro Gly Ala Arg Gln
180 185 190

Gly Gln Gln Gln Ala Gly Gly Asp Gly Lys Thr Glu Gln Lys Gly Gly
195 200 205

Asp Lys Lys Arg Gly Val Lys Arg Pro Arg Glu Asp His Gly Arg Gly
210 215 220

Tyr Phe Glu Tyr Ile Glu Glu Asn Lys Tyr Ser Arg Ala Lys Ser Pro
225 230 235 240

Gln Pro Pro Val Glu Glu Glu Asp Glu His Phe Asp Asp Thr Val Val
245 250 255

Cys Leu Asp Thr Tyr Asn Cys Asp Leu His Phe Lys Ile Ser Arg Asp
260 265 270

Arg Leu Ser Ala Ser Ser Leu Thr Met Glu Ser Phe Ala Phe Leu Trp
275 280 285

Ala Gly Gly Arg Ala Ser Tyr Gly Val Ser Lys Gly Lys Val Cys Phe
290 295 300

Glu Met Lys Val Thr Glu Lys Ile Pro Val Arg His Leu Tyr Thr Lys
 305 310 315 320

Asp Ile Asp Ile His Glu Val Arg Ile Gly Trp Ser Leu Thr Thr Ser
 325 330 335

Gly Met Leu Leu Gly Glu Glu Glu Phe Ser Tyr Gly Tyr Ser Leu Lys
 340 345 350

Gly Ile Lys Thr Cys Asn Cys Glu Thr Glu Asp Tyr Gly Glu Lys Phe
 355 360 365

Asp Glu Asn Asp Val Ile Thr Cys Phe Ala Asn Phe Glu Ser Asp Glu
 370 375 380

Val Glu Leu Ser Tyr Ala Lys Asn Gly Gln Asp Leu Gly Val Ala Phe
 385 390 395 400

Lys Ile Ser Lys Glu Val Leu Ala Gly Arg Pro Leu Phe Pro His Val
 405 410 415

Leu Cys His Asn Cys Ala Val Glu Phe Asn Phe Gly Gln Lys Glu Lys
 420 425 430

Pro Tyr Phe Pro Ile Pro Glu Glu Tyr Thr Phe Ile Gln Asn Val Pro
 435 440 445

Leu Glu Asp Arg Val Arg Gly Pro Lys Gly Pro Glu Glu Lys Lys Asp
 450 455 460

Cys Glu Val Val Met Met Ile Gly Leu Pro Gly Ala Gly Lys Thr Thr
 465 470 475 480

Trp Val Thr Lys His Ala Ala Glu Asn Pro Gly Lys Tyr Asn Ile Leu
 485 490 495

Gly Thr Asn Thr Ile Met Asp Lys Met Met Val Ala Gly Phe Lys Lys
 500 505 510

Gln Met Ala Asp Thr Gly Lys Leu Asn Thr Leu Leu Gln Arg Ala Pro
 515 520 525

Gln Cys Leu Gly Lys Phe Ile Glu Ile Ala Ala Arg Lys Lys Arg Asn
 530 535 540

322/383

Phe Ile Leu Asp Gln Thr Asn Val Ser Ala Ala Ala Gln Arg Arg Lys
 545 550 555 560

Met Cys Leu Phe Ala Gly Phe Gln Arg Lys Ala Val Val Val Cys Pro
 565 570 575

Lys Asp Glu Asp Tyr Lys Gln Arg Thr Gln Lys Lys Ala Glu Val Glu
 580 585 590

Gly Lys Asp Leu Pro Glu His Ala Val Leu Lys Met Lys Gly Asn Phe
 595 600 605

Thr Leu Pro Glu Val Ala Glu Cys Phe Asp Glu Ile Thr Tyr Val Glu
 610 615 620

Leu Gln Lys Glu Glu Ala Gln Lys Leu Leu Glu Gln Tyr Lys Glu Glu
 625 630 635 640

Ser Lys Lys Ala Leu Pro Pro Glu Lys Lys Gln Asn Thr Gly Ser Lys
 645 650 655

Lys Ser Asn Lys Asn Lys Ser Gly Lys Asn Gln Phe Asn Arg Gly Gly
 660 665 670

Gly His Arg Gly Arg Gly Gly Phe Asn Met Arg Gly Gly Asn Phe Arg
 675 680 685

Gly Gly Ala Pro Gly Asn Arg Gly Gly Tyr Asn Arg Arg Gly Asn Met
 690 695 700

Pro Gln Arg Gly Gly Gly Gly Gly Gly Ser Gly Gly Ile Gly Tyr Pro
 705 710 715 720

Tyr Pro Arg Ala Pro Val Phe Pro Gly Arg Gly Ser Tyr Ser Asn Arg
 725 730 735

Gly Asn Tyr Asn Arg Gly Gly Met Pro Asn Arg Gly Asn Tyr Asn Gln
 740 745 750

Asn Phe Arg Gly Arg Gly Asn Asn Arg Gly Tyr Lys Asn Gln Ser Gln
 755 760 765

Gly Tyr Asn Gln Trp Gln Gln Gly Gln Phe Trp Gly Gln Lys Pro Trp
 770 775 780

Ser Gln His Tyr His Gln Gly Tyr Tyr

323/383

785

790

<210> 202
 <211> 325
 <212> PRT
 <213> Homo sapien

<400> 202

Met Ile Phe Arg Asp Phe Ile Phe Ala Gln Val Ile Ser Lys Tyr Glu
 1 5 10 15

Asp Ile Phe Phe Val Phe Phe Gln Val Gly Cys Leu Lys Phe Phe Pro
 20 25 30

Phe Phe Ile Pro Leu Pro Lys Ala Asn Glu Lys Lys Val Asp Gln Pro
 35 40 45

Pro Glu Ala Lys Lys Pro Lys Ile Lys Val Val Asn Val Glu Leu Pro
 50 55 60

Ile Glu Ala Asn Leu Val Trp Gln Leu Gly Lys Asp Leu Leu Asn Met
 65 70 75 80

Tyr Ile Glu Thr Glu Gly Lys Met Ile Met Gln Asp Lys Leu Glu Lys
 85 90 95

Glu Arg Asn Asp Ala Lys Asn Ala Val Glu Glu Tyr Val Tyr Glu Phe
 100 105 110

Arg Asp Lys Leu Cys Gly Pro Tyr Glu Lys Phe Ile Cys Glu Gln Asp
 115 120 125

His Gln Asn Phe Leu Arg Leu Leu Thr Glu Thr Glu Asp Trp Leu Tyr
 130 135 140

Glu Glu Gly Glu Asp Gln Ala Lys Gln Ala Tyr Val Asp Lys Leu Glu
 145 150 155 160

Glu Leu Met Lys Ile Gly Thr Pro Val Lys Val Arg Phe Gln Glu Ala
 165 170 175

Glu Glu Arg Pro Lys Met Phe Glu Glu Leu Gly Gln Arg Leu Gln His
 180 185 190

Tyr Ala Lys Ile Ala Ala Asp Phe Arg Asn Lys Asp Glu Lys Tyr Asn
 195 200 205

His Ile Asp Glu Ser Glu Met Lys Lys Val Glu Lys Ser Val Asn Glu
 210 215 220

Val Met Glu Trp Met Asn Asn Val Met Asn Ala Gln Ala Lys Lys Ser
 225 230 235 240

Leu Asp Gln Asp Pro Val Val Arg Ala Gln Glu Ile Lys Thr Lys Ile
 245 250 255

Lys Glu Leu Asn Asn Thr Cys Glu Pro Val Val Thr Gln Pro Lys Pro
 260 265 270

Lys Ile Glu Ser Pro Lys Leu Glu Arg Thr Pro Asn Gly Pro Asn Ile
 275 280 285

Asp Lys Lys Glu Glu Asp Leu Glu Asp Lys Asn Asn Phe Gly Ala Glu
 290 295 300

Pro Pro His Gln Asn Gly Glu Cys Tyr Pro Asn Glu Lys Asn Ser Val
 305 310 315 320

Asn Met Asp Leu Asp
 325

<210> 203
 <211> 131
 <212> PRT
 <213> Homo sapien

<400> 203

Met Lys Val Gln Asn Arg Arg Asn Ala His Leu Ser Ser Phe Asp Arg
 1 5 10 15

Phe Ala Phe Leu Trp Glu Met Gln Phe Arg Val Thr Cys Cys Arg Arg
 20 25 30

Tyr Val Val Asp His Leu Asp Ile Ile Ala Glu Asp Glu Leu Leu Asp
 35 40 45

Gln Leu Leu Ser His Thr Ala Ser Leu Ser Asp Leu Leu Gln Asn Ser
 50 55 60

Val Val Ala Thr Ala Gln Thr Arg Leu Arg Ser Tyr Ser Cys Ala Ser
 65 70 75 80

Leu Arg Phe Ser Ser Ala Thr Met Ser Asp Lys Pro Asp Met Ala Glu

325/383

85

90

95

Ile Glu Lys Phe Asp Lys Ser Lys Leu Lys Lys Thr Glu Thr Gln Glu
 100 105 110

Lys Asn Pro Leu Pro Ser Lys Glu Thr Ile Glu Gln Glu Lys Gln Ala
 115 120 125

Gly Glu Ser
 130

<210> 204
 <211> 116
 <212> PRT
 <213> Homo sapien

<400> 204

Ser Leu Arg Leu Pro Trp Glu Met Gln Phe Arg Val Thr Cys Cys Arg
 1 5 10 15

Arg Tyr Val Val Asp His Leu Asp Ile Ile Ala Glu Asp Glu Leu Leu
 20 25 30

Asp Gln Leu Leu Ser His Thr Ala Ser Leu Ser Asp Leu Leu Gln Asn
 35 40 45

Ser Val Val Ala Thr Ala Gln Thr Arg Leu Arg Ser Tyr Ser Cys Ala
 50 55 60

Ser Leu Arg Phe Ser Ser Ala Thr Met Ser Asp Lys Pro Asp Met Ala
 65 70 75 80

Glu Ile Glu Lys Phe Asp Lys Ser Lys Leu Lys Lys Thr Glu Thr Gln
 85 90 95

Glu Lys Asn Pro Leu Pro Ser Lys Glu Thr Ile Glu Gln Glu Lys Gln
 100 105 110

Ala Gly Glu Ser
 115

<210> 205
 <211> 63
 <212> PRT
 <213> Homo sapien

<400> 205

326/383

Met Cys Leu Gly Val Cys Ser Phe Arg Cys Ser Asp Met Ser Arg Val
 1 5 10 15

Ser Ser Phe Gln Trp Val Arg Gly Leu Thr Asp Phe Arg Asn Glu Ala
 20 25 30

Ala Tyr Ala His Ala Pro Gln Lys Ser Ser Pro Ser Pro His Ser Thr
 35 40 45

Gln Glu Val Leu Leu Ser Ser Pro Val Thr Ser Tyr Trp Gly Gly
 50 55 60

<210> 206
 <211> 97
 <212> PRT
 <213> Homo sapien

<400> 206

Cys Val Ser Glu Phe Val Pro Ser Asp Val Gln Ile Cys Pro Glu Phe
 1 5 10 15

Leu Pro Ser Ser Gly Phe Val Val Ser Leu Thr Ser Gly Met Lys Leu
 20 25 30

His Thr Leu Thr Leu His Arg Lys Val Leu Gln Val Pro Thr Arg Pro
 35 40 45

Arg Lys Ser Cys Cys Leu His Leu Ser Pro Ala Thr Gly Glu Ala Glu
 50 55 60

Ala Gly Glu Ser Leu Glu Pro Arg Arg Trp Arg Leu Leu Gly Ala Lys
 65 70 75 80

Pro Arg Ser Arg His Tyr Thr Pro Ala Trp Gln Gln Ser Glu Thr Pro
 85 90 95

Ser

<210> 207
 <211> 163
 <212> PRT
 <213> Homo sapien

<400> 207

Met Asn Gly Glu Tyr Tyr Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr
 1 5 10 15

Ala Ala Ile Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile
20 25 30

Arg Lys Trp Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala
35 40 45

Asn Ser Arg Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu
50 55 60

Leu Glu Glu Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys
65 70 75 80

Ala Asn Asn Arg Ala Ala Glu Glu Ala Phe Val Asn Asp Ile Asp Glu
85 90 95

Ser Ser Pro Gly Thr Glu Trp Glu Arg Val Ala Arg Leu Cys Asp Phe
100 105 110

Asn Pro Lys Ser Ser Lys Gln Ala Lys Asp Val Phe Pro Pro Cys Ala
115 120 125

Gln Ser Ser Ser Pro Ser Ser Arg Pro Leu Val Leu Glu Ala Pro Val
130 135 140

Asp Leu Leu Val Leu Pro Arg Gly Leu Arg Trp Val Leu Gly Trp Pro
145 150 155 160

Leu Leu Ala

<210> 208

<211> 283

<212> PRT

<213> Homo sapien

<400> 208

Arg Leu Gly Thr Arg Leu Gly Val Ala Pro Leu Pro Val Gly Thr Thr
1 5 10 15

Ala Val Ala Ala Gly Arg Gly Val Gly Gly Ser Val Gly Phe Cys Leu
20 25 30

Thr Val Gly Val Arg Ala Val Gln Leu Pro Ala Met Ala Glu Leu Asp
35 40 45

Pro Phe Gly Ala Pro Ala Gly Ala Pro Gly Gly Pro Ala Leu Gly Asn

328/383

50 55 60
 Gly Val Ala Gly Ala Gly Glu Glu Asp Pro Ala Ala Ala Phe Leu Ala
 65 70 75 80
 Gln Gln Glu Ser Glu Ile Ala Gly Ile Glu Asn Asp Glu Ala Phe Ala
 85 90 95
 Ile Leu Asp Gly Gly Ala Pro Gly Pro Gln Pro His Gly Glu Pro Pro
 100 105 110
 Gly Gly Pro Asp Ala Val Asp Gly Val Met Asn Gly Glu Tyr Tyr Gln
 115 120 125
 Glu Ser Asn Gly Pro Thr Asp Ser Tyr Ala Ala Ile Ser Gln Val Asp
 130 135 140
 Arg Leu Gln Ser Glu Pro Glu Ser Ile Arg Lys Trp Arg Glu Glu Gln
 145 150 155 160
 Met Glu Arg Leu Glu Ala Leu Asp Ala Asn Ser Arg Lys Gln Glu Ala
 165 170 175
 Glu Trp Lys Glu Lys Ala Ile Lys Glu Leu Glu Glu Trp Tyr Ala Arg
 180 185 190
 Gln Asp Glu Gln Leu Gln Lys Thr Lys Ala Asn Asn Arg Ala Ala Glu
 195 200 205
 Glu Ala Phe Val Asn Asp Ile Asp Glu Ser Ser Pro Gly Thr Glu Trp
 210 215 220
 Glu Arg Val Ala Arg Leu Cys Asp Phe Asn Pro Lys Ser Ser Lys Gln
 225 230 235 240
 Ala Lys Asp Val Ser Arg Met Arg Ser Val Leu Ile Ser Leu Lys Gln
 245 250 255
 Ala Ala Gly Ala Gly Gly Pro Val Asp Leu Leu Val Leu Pro Arg Gly
 260 265 270
 Leu Arg Trp Val Leu Gly Trp Pro Leu Leu Ala
 275 280
 <210> 209
 <211> 222

<212> PRT

<213> Homo sapien

<400> 209

Met Ala Glu Leu Asp Pro Phe Gly Ala Pro Ala Gly Ala Pro Gly Gly
 1 5 10 15

Pro Ala Leu Gly Asn Gly Val Ala Gly Ala Gly Glu Glu Asp Pro Ala
 20 25 30

Ala Ala Phe Leu Ala Gln Gln Glu Ser Glu Ile Ala Gly Ile Glu Asn
 35 40 45

Asp Glu Ala Phe Ala Ile Leu Asp Gly Ala Ala Pro Pro Gly Pro Ser
 50 55 60

Arg Thr Ala Ser Arg Arg Gly Val Arg Met Gln Glu Ser Asn Gly Pro
 65 70 75 80

Thr Asp Ser Tyr Ala Ala Ile Ser Gln Val Asp Arg Leu Gln Ser Glu
 85 90 95

Pro Glu Ser Ile Arg Lys Trp Arg Glu Glu Gln Met Glu Arg Leu Glu
 100 105 110

Ala Leu Asp Ala Asn Ser Arg Lys Gln Glu Ala Glu Trp Lys Glu Lys
 115 120 125

Ala Ile Lys Glu Leu Glu Glu Trp Tyr Ala Arg Gln Asp Glu Gln Leu
 130 135 140

Gln Lys Thr Lys Ala Asn Asn Arg Ala Ala Glu Glu Ala Phe Val Asn
 145 150 155 160

Asp Ile Asp Glu Ser Ser Pro Gly Thr Glu Trp Glu Arg Val Ala Arg
 165 170 175

Leu Cys Asp Phe Asn Pro Lys Ser Ser Lys Gln Ala Lys Asp Val Phe
 180 185 190

Pro Pro Cys Ala Gln Ser Ser Ser Pro Ser Ser Arg Pro Arg Trp Cys
 195 200 205

Thr Glu Glu Pro Pro Cys Gly Asn Thr Thr Ser Ala Ile Ser
 210 215 220

<210> 210
 <211> 250
 <212> PRT
 <213> Homo sapien

<400> 210

Asn Arg Thr Arg Gly Ala Leu Val Leu Leu Ser Gln Ser Ala Pro Gln
 1 5 10 15

Arg Trp Leu Pro Gly Val Val Ser Val Gly Arg Leu Val Phe Val Ser
 20 25 30

Pro Leu Val Ser Val Pro Phe Ser Cys Pro Pro Trp Leu Ser Trp Ile
 35 40 45

Arg Ser Ala Pro Leu Pro Ala Pro Leu Ala Val Pro Arg Trp Gly Thr
 50 55 60

Glu Trp Pro Ala Pro Ala Lys Lys Thr Arg Leu Arg Pro Ser Trp Arg
 65 70 75 80

Ser Lys Arg Ala Arg Leu Arg Ala Ser Arg Thr Thr Arg Pro Ser Pro
 85 90 95

Ser Trp Thr Ala Ala Pro Pro Gly Pro Ser Arg Thr Ala Ser Arg Arg
 100 105 110

Gly Val Arg Met Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr Ala Ala
 115 120 125

Ile Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile Arg Lys
 130 135 140

Trp Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala Asn Ser
 145 150 155 160

Arg Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu Leu Glu
 165 170 175

Glu Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys Ala Asn
 180 185 190

Asn Arg Ala Ala Glu Glu Ala Phe Val Asn Asp Ile Asp Glu Ser Ser
 195 200 205

Pro Gly Thr Glu Trp Glu Arg Val Ala Arg Leu Cys Asp Phe Asn Pro
 210 215 220

Lys Ser Ser Lys Gln Ala Lys Asp Val Ser Arg Met Arg Ser Val Leu
 225 230 235 240

Ile Ser Leu Lys Gln Ala Pro Leu Val His
 245 250

<210> 211
 <211> 142
 <212> PRT
 <213> Homo sapien

<400> 211

Ser Ser Arg Ser Arg Ala Ala Ala Arg Asp Leu Glu Pro Asp Ala Trp
 1 5 10 15

Gly Ala Cys Pro Pro Leu Pro Val Gly Thr Thr Ala Val Ala Ala Gly
 20 25 30

Arg Gly Val Gly Gly Ser Val Gly Phe Cys Leu Thr Val Gly Val Arg
 35 40 45

Ala Val Gln Leu Pro Ala Met Ala Glu Leu Asp Pro Phe Gly Ala Pro
 50 55 60

Ala Gly Ala Pro Gly Gly Pro Ala Leu Gly Asn Gly Val Ala Gly Ala
 65 70 75 80

Gly Glu Glu Asp Pro Ala Ala Ala Phe Leu Ala Gln Gln Glu Ser Glu
 85 90 95

Ile Ala Gly Ile Glu Asn Asp Glu Ala Phe Ala Ile Leu Asp Gly Ala
 100 105 110

Ala Pro Pro Gly Pro Ser Arg Thr Ala Ser Arg Arg Gly Val Arg Met
 115 120 125

Pro Ile Leu Gly Ser Lys Lys Gln Ser Gly Lys Lys Arg Gln
 130 135 140

<210> 212
 <211> 220
 <212> PRT
 <213> Homo sapien

<400> 212

Ser Ser Arg Ser Arg Ala Ala Ala Arg Asp Leu Glu Pro Asp Ala Trp

332/383

[illegible]

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<210> 213
<211> 111
<212> PRT
<213> Homo sapien
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<400> 213

Met Asn Gly Glu Tyr Tyr Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr
1 5 10 15

Ala Ala Ile Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile
20 25 30

Arg Lys Trp Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala
35 40 45

Asn Ser Arg Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu
50 55 60

Leu Glu Glu Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys
65 70 75 80

Ala Asn Asn Arg Val Ala Asp Glu Ala Phe Tyr Lys Gln Pro Phe Ala
85 90 95

Asp Val Ile Gly Tyr Val Gln Gly Ser Arg Arg Ser Leu Cys Lys
100 105 110

<210> 214
<211> 236
<212> PRT
<213> Homo sapien

<400> 214

Gly Phe Arg Phe Thr Arg Leu Pro Pro Gly Ala Cys Pro Pro Leu Pro
1 5 10 15

Val Gly Thr Thr Ala Val Ala Ala Gly Arg Gly Val Gly Gly Ser Val
20 25 30

Gly Phe Cys Leu Thr Val Gly Val Arg Ala Val Gln Leu Pro Ala Met
35 40 45

Ala Glu Leu Asp Pro Phe Gly Ala Pro Ala Gly Ala Pro Gly Gly Pro
50 55 60

Ala Leu Gly Asn Gly Val Ala Gly Ala Gly Glu Glu Asp Pro Ala Ala
65 70 75 80

Ala Phe Leu Ala Gln Gln Glu Ser Glu Ile Ala Gly Ile Glu Asn Asp
85 90 95

Glu Ala Phe Ala Ile Leu Asp Gly Gly Ala Pro Gly Pro Gln Pro His

100 105 110
 Gly Glu Pro Pro Gly Gly Pro Asp Ala Val Asp Gly Val Met Asn Gly
 115 120 125
 Glu Tyr Tyr Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr Ala Ala Ile
 130 135 140
 Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile Arg Lys Trp
 145 150 155 160
 Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala Asn Ser Arg
 165 170 175
 Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu Leu Glu Glu
 180 185 190
 Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys Ala Asn Asn
 195 200 205
 Arg Val Ala Asp Glu Ala Phe Tyr Lys Gln Pro Phe Ala Asp Val Ile
 210 215 220
 Gly Tyr Val Gln Gly Ser Arg Arg Ser Leu Cys Lys
 225 230 235
 <210> 215
 <211> 211
 <212> PRT
 <213> Homo sapien
 <400> 215
 Met Asn Gly Glu Tyr Tyr Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr
 1 5 10 15
 Ala Ala Ile Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile
 20 25 30
 Arg Lys Trp Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala
 35 40 45
 Asn Ser Arg Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu
 50 55 60
 Leu Glu Glu Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys
 65 70 75 80

Ala Asn Asn Arg Ala Ala Glu Glu Ala Phe Val Asn Asp Ile Asp Glu
85 90 95

Ser Ser Pro Gly Thr Glu Trp Glu Arg Val Ala Arg Leu Cys Asp Phe
100 105 110

Asn Pro Lys Ser Ser Lys Gln Ala Lys Asp Val Phe Pro Pro Cys Ala
115 120 125

Gln Ser Ser Ser Pro Ser Ser Arg Pro Val Gly Asp Glu Glu His Leu
130 135 140

Trp Lys Thr Asn Leu Ile Phe Ile Tyr Gln Gly Ser Leu Ser Met Ile
145 150 155 160

Tyr Val Glu Val Leu Glu Asn Leu Cys Ser Ser Val Leu Leu Val Gly
165 170 175

Phe Ser Lys Gly Ser Gly Lys Arg Gly Arg Lys Gly Ala Lys Arg Trp
180 185 190

Phe Lys Phe Gly Arg Lys Lys Lys Gly Leu Gly Cys Phe Val Gly Leu
195 200 205

Lys Phe Ile
210

<210> 216
<211> 263
<212> PRT
<213> Homo sapien

<220>
<221> MISC_FEATURE
<222> (263)..(263)
<223> X=any amino acid

<400> 216

Gly Phe Arg Phe Thr Arg Leu Pro Pro Gly Ala Cys Pro Pro Leu Pro
1 5 10 15

Val Gly Thr Thr Ala Val Ala Ala Gly Arg Gly Val Gly Gly Ser Val
20 25 30

Gly Phe Cys Leu Thr Val Gly Val Arg Ala Val Gln Leu Pro Ala Met
35 40 45

Ala Glu Leu Asp Pro Phe Gly Ala Pro Ala Gly Ala Pro Gly Gly Pro
 50 55 60

Ala Leu Gly Asn Gly Val Ala Gly Ala Gly Glu Glu Asp Pro Ala Ala
 65 70 75 80

Ala Phe Leu Ala Gln Gln Glu Ser Glu Ile Ala Gly Ile Glu Asn Asp
 85 90 95

Glu Ala Phe Ala Ile Leu Asp Gly Gly Ala Pro Gly Pro Gln Pro His
 100 105 110

Gly Glu Pro Pro Gly Gly Pro Asp Ala Val Asp Gly Val Met Asn Gly
 115 120 125

Glu Tyr Tyr Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr Ala Ala Ile
 130 135 140

Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile Arg Lys Trp
 145 150 155 160

Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala Asn Ser Arg
 165 170 175

Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu Leu Glu Glu
 180 185 190

Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys Ala Asn Asn
 195 200 205

Arg Ala Ala Glu Glu Ala Phe Val Asn Asp Ile Asp Glu Ser Ser Pro
 210 215 220

Gly Thr Glu Trp Glu Arg Val Ala Arg Leu Cys Asp Phe Asn Pro Lys
 225 230 235 240

Ser Ser Lys Gln Ala Lys Asp Val Ser Arg Met Arg Ser Val Leu Ile
 245 250 255

Ser Leu Lys Gln Ala Arg Xaa
 260

<210> 217

<211> 150

<212> PRT

<213> Homo sapien

<400> 217

Met Asn Gly Glu Tyr Tyr Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr
 1 5 10 15

Ala Ala Ile Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile
 20 25 30

Arg Lys Trp Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala
 35 40 45

Asn Ser Arg Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu
 50 55 60

Leu Glu Glu Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys
 65 70 75 80

Ala Asn Asn Arg Ala Ala Glu Glu Ala Phe Val Asn Asp Ile Asp Glu
 85 90 95

Ser Ser Pro Gly Thr Glu Trp Glu Arg Val Ala Arg Leu Cys Asp Phe
 100 105 110

Asn Pro Lys Ser Ser Lys Arg Ala Arg Cys Phe Pro Met Ala Gln Thr
 115 120 125

His Ser Ser Arg Arg Pro Val Cys Leu Arg Ala Pro Val Glu Pro Thr
 130 135 140

Leu Ile Phe Ile Tyr Gln
 145 150

<210> 218

<211> 269

<212> PRT

<213> Homo sapien

<400> 218

Gly Phe Arg Phe Thr Arg Leu Pro Pro Gly Ala Cys Pro Pro Leu Pro
 1 5 10 15

Val Gly Thr Thr Ala Val Ala Ala Gly Arg Gly Val Gly Gly Ser Val
 20 25 30

Gly Phe Cys Leu Thr Val Gly Val Arg Ala Val Gln Leu Pro Ala Met
 35 40 45

Ala Glu Leu Asp Pro Phe Gly Ala Pro Ala Gly Ala Pro Gly Gly Pro
 50 55 60

Ala Leu Gly Asn Gly Val Ala Gly Ala Gly Glu Glu Asp Pro Ala Ala
 65 70 75 80

Ala Phe Leu Ala Gln Gln Glu Ser Glu Ile Ala Gly Ile Glu Asn Asp
 85 90 95

Glu Ala Phe Ala Ile Leu Asp Gly Gly Ala Pro Gly Pro Gln Pro His
 100 105 110

Gly Glu Pro Pro Gly Gly Pro Asp Ala Val Asp Gly Val Met Asn Gly
 115 120 125

Glu Tyr Tyr Gln Glu Ser Asn Gly Pro Thr Asp Ser Tyr Ala Ala Ile
 130 135 140

Ser Gln Val Asp Arg Leu Gln Ser Glu Pro Glu Ser Ile Arg Lys Trp
 145 150 155 160

Arg Glu Glu Gln Met Glu Arg Leu Glu Ala Leu Asp Ala Asn Ser Arg
 165 170 175

Lys Gln Glu Ala Glu Trp Lys Glu Lys Ala Ile Lys Glu Leu Glu Glu
 180 185 190

Trp Tyr Ala Arg Gln Asp Glu Gln Leu Gln Lys Thr Lys Ala Asn Asn
 195 200 205

Arg Ala Ala Glu Glu Ala Phe Val Asn Asp Ile Asp Glu Ser Ser Pro
 210 215 220

Gly Thr Glu Trp Glu Arg Val Ala Arg Leu Cys Asp Phe Asn Pro Lys
 225 230 235 240

Ser Ser Lys Arg Ala Arg Cys Phe Pro Met Ala Gln Ser His Ser Ser
 245 250 255

Arg Arg Pro Val Cys Leu Arg Ala Leu Trp Asn Leu His
 260 265

<210> 219

<211> 152

<212> PRT

<213> Homo sapien

<400> 219

Met Lys Ala Leu Ile Val Leu Gly Leu Val Leu Leu Ser Val Thr Val
1 5 10 15

Gln Gly Lys Val Phe Glu Arg Cys Glu Leu Ala Arg Thr Leu Lys Arg
20 25 30

Leu Gly Met Asp Gly Tyr Arg Gly Ile Ser Leu Ala Asn Trp Met Cys
35 40 45

Leu Ala Lys Trp Glu Ser Gly Tyr Asn Thr Arg Ala Thr Asn Tyr Asn
50 55 60

Ala Gly Asp Arg Ser Thr Asp Tyr Gly Ile Phe Gln Ile Asn Ser Arg
65 70 75 80

Tyr Trp Cys Asn Asp Gly Lys Thr Pro Gly Ala Val Asn Ala Cys His
85 90 95

Leu Ser Cys Ser Ala Leu Leu Gln Asp Asn Ile Ala Asp Ala Val Ala
100 105 110

Cys Ala Lys Arg Val Val Arg Asp Pro Gln Gly Ile Arg Ala Trp Val
115 120 125

Ala Trp Arg Asn Arg Cys Leu Ser Phe Phe Ser Ser Phe Cys Leu Ser
130 135 140

His Ile Lys Gly Val Gly Ile Lys
145 150

<210> 220

<211> 178

<212> PRT

<213> Homo sapien

<400> 220

Ser Glu Gly Gly Ala Trp Thr Pro Gly Ser Glu Pro Thr Gly Ala Gln
1 5 10 15

Ala Cys Glu Phe Glu Ala Pro Ser His His Pro Pro Pro Gln Val Val
20 25 30

Tyr Ile Ala Cys Ser Phe Thr Thr Val Trp Leu Ile Tyr Ser Lys Phe
35 40 45

Lys Ala Thr Tyr Asp Gly Asn His Asp Thr Phe Arg Val Glu Phe Leu
 50 55 60

Val Val Pro Thr Ala Ile Leu Ala Phe Leu Val Asn His Asp Phe Thr
 65 70 75 80

Pro Leu Glu Ile Leu Trp Thr Phe Ser Ile Tyr Leu Glu Ser Val Ala
 85 90 95

Ile Leu Pro Gln Leu Phe Met Val Ser Lys Thr Gly Glu Ala Glu Thr
 100 105 110

Ile Thr Ser His Tyr Leu Phe Ala Leu Gly Val Tyr Arg Thr Leu Tyr
 115 120 125

Leu Phe Asn Trp Ile Trp Arg Tyr His Phe Glu Gly Phe Phe Asp Leu
 130 135 140

Ile Ala Ile Val Ala Gly Leu Val Gln Thr Val Leu Tyr Cys Asp Phe
 145 150 155 160

Phe Tyr Leu Tyr Ile Thr Lys Val Leu Lys Gly Lys Lys Leu Ser Leu
 165 170 175

Pro Ala

<210> 221
 <211> 183
 <212> PRT
 <213> Homo sapien

<400> 221

Leu His Pro Ser Gly Asp Pro Leu Asp Leu Leu His Leu Pro Gly Val
 1 5 10 15

Ser Gly His Leu Ala Ala Ala Val His Gly Glu Gln Asp Arg Arg Gly
 20 25 30

Gly Asp His His Gln Pro Leu Leu Val Cys Ala Arg Arg Leu Pro His
 35 40 45

Ala Leu Ser Leu Gln Leu Asp Leu Ala Leu Pro Phe Arg Gly Leu Leu
 50 55 60

Arg Pro His Arg His Cys Gly Arg Pro Gly Pro Asp Ser Pro Leu Leu

Lys Lys Ala Ser Ser Ser Asp Ser Glu Asp Ser Ser Glu Glu Glu Glu
85 90 95

Glu Val Gln Gly Pro Pro Ala Lys Lys Ala Ala Val Pro Ala Lys Arg
 100 105 110

Val Gly Leu Pro Pro Gly Lys Ala Ala Ala Lys Ala Ser Glu Ser Ser
 115 120 125

Ser Ser Glu Glu Ser Ser Asp Asp Asp Asp Glu Glu Asp Gln Lys Lys
 130 135 140

Gln Pro Val Gln Lys Gly Val Lys Pro Gln Ala Lys Ala Ala Lys Ala
 145 150 155 160

Pro Pro Lys Lys Ala Lys Ser Ser Asp Ser Asp Ser Asp Ser Ser Ser
 165 170 175

Glu Asp Glu Pro Pro Lys Asn Gln Lys Pro Lys Ile Thr Pro Val Thr
 180 185 190

Val Lys Ala Gln Thr Lys Ala Pro Pro Lys Pro Ala Arg Ala Ala Pro
 195 200 205

Lys Ile Ala Asn Gly Lys Ala Ala Ser Ser Ser Ser Ser Ser Ser Ser
 210 215 220

Ser Ser Ser Ser Asp Asp Ser Glu Glu Glu Lys Ala Ala Ala Thr Pro
 225 230 235 240

Lys Lys Val Trp Thr Ile Thr Ser Val Arg Ala Glu Val Thr Arg Ala
 245 250 255

Val Met Cys Val Cys Leu Pro Ser Leu Ala Gly Leu Val Gly Ser Ala
 260 265 270

Phe Ser Cys Gly Glu Ser Ile Phe Phe Leu Met Gln Thr Val Pro Lys
 275 280 285

Lys Gln Val Val Ala Lys Ala Pro Val Lys Ala Ala Thr Thr Pro Thr
 290 295 300

Arg Lys Ser Ser Ser Ser Glu Asp Ser Ser Ser Asp Glu Glu Glu Glu
 305 310 315 320

Gln Lys Lys Pro Met Lys Asn Lys Pro Gly Pro Tyr Ser Ser Val Pro
 325 330 335

Pro Pro Ser Ala Pro Pro Pro Lys Lys Ser Leu Gly Thr Gln Pro Pro
340 345 350

Lys Lys Ala Val Glu Lys Gln Gln Pro Val Glu Ser Ser Glu Asp Ser
355 360 365

Ser Asp Glu Ser Asp Ser Ser Ser Glu Glu Glu Lys Lys Pro Pro Thr
370 375 380

Lys Ala Val Val Ser Lys Ala Thr Thr Lys Pro Pro Pro Ala Lys Lys
385 390 395 400

Ala Ala Glu Ser Ser Ser Asp Ser Ser Asp Ser Asp Ser Ser Glu Asp
405 410 415

Asp Glu Ala Pro Ser Lys Pro Ala Gly Thr Thr Lys Asn Ser Ser Asn
420 425 430

Lys Pro Ala Val Thr Thr Lys Ser Pro Ala Val Lys Pro Ala Ala Ala
435 440 445

Pro Lys Gln Pro Val Gly Gly Gly Gln Lys Leu Leu Thr Arg Lys Ala
450 455 460

Asp Ser Ser Ser Ser Glu Glu Glu Ser Ser Ser Ser Glu Glu Glu Lys
465 470 475 480

Thr Lys Lys Met Val Ala Thr Thr Lys Pro Lys Ala Thr Ala Lys Ala
485 490 495

Ala Leu Ser Leu Pro Ala Lys Gln Ala Pro Gln Gly Ser Arg Asp Ser
500 505 510

Ser Ser Asp Ser Asp Ser Ser Ser Glu Glu Glu Glu Glu Lys Thr
515 520 525

Ser Lys Ser Ala Val Lys Lys Lys Pro Gln Lys Val Ala Gly Gly Ala
530 535 540

Ala Pro Ser Lys Pro Ala Ser Ala Lys Lys Gly Lys Ala Glu Ser Ser
545 550 555 560

Asn Ser Ser Ser Ser Asp Asp Ser Ser Glu Glu Glu Glu Glu Lys Leu
565 570 575

Lys Gly Lys Gly Ser Pro Arg Pro Gln Ala Pro Lys Ala Asn Gly Thr

Lys His Tyr Gln Lys Gln Gln Ser Leu Pro Ser Leu Cys Ser Thr Ser
35 40 45

Asp Pro Asp Thr Pro Leu Gly Ala Pro Ser Ser Ser Asp Ser Asp Ser
50 55 60

Ser Ser Ser Glu Glu Glu Glu Glu Lys Thr Ser Lys Ser Ala Val Lys
65 70 75 80

Lys Lys Pro Gln Lys Val Ala Gly Gly Ala Ala Pro Ser Lys Pro Ala
85 90 95

Ser Ala Lys Lys Gly Lys Ala Glu Ser Ser Asn Ser Ser Ser Ser Asp
100 105 110

Asp Ser Ser Glu Glu Glu Glu Glu Lys Leu Lys Gly Lys Gly Ser Pro
115 120 125

Arg Pro Gln Ala Pro Lys Ala Asn Gly Thr Ser Ala Leu Thr Ala Gln
130 135 140

Asn Gly Lys Ala Ala Lys Asn Ser Glu Glu Glu Glu Glu Lys Lys
145 150 155 160

Lys Ala Ala Val Val Val Ser Lys Ser Gly Ser Leu Lys Lys Arg Lys
165 170 175

Gln Asn Glu Ala Ala Lys Glu Ala Glu Thr Pro Gln Ala Lys Lys Ile
180 185 190

Lys Leu Gln Thr Pro Asn Thr Phe Pro Lys Arg Lys Lys Gly Glu Lys
195 200 205

Arg Ala Ser Ser Pro Phe Arg Arg Val Arg Glu Glu Glu Ile Glu Val
210 215 220

Asp Ser Arg Val Ala Asp Asn Ser Phe Asp Ala Lys Arg Gly Ala Ala
225 230 235 240

Gly Asp Trp Gly Glu Arg Ala Asn Gln Val Leu Lys Phe Thr Lys Gly
245 250 255

Lys Ser Phe Arg His Glu Lys Thr Lys Lys Lys Arg Gly Ser Tyr Arg
260 265 270

Gly Gly Ser Ile Ser Val Gln Val Asn Ser Ile Lys Phe Asp Ser Glu
275 280 285

<210> 224
 <211> 265
 <212> PRT
 <213> Homo sapien

<400> 224

Ser Ser Ala Pro Asp Phe Ala Asn Leu Lys His Tyr Gln Lys Gln Gln
 1 5 10 15

Ser Leu Pro Ser Leu Cys Ser Thr Ser Asp Pro Asp Thr Pro Leu Gly
 20 25 30

Ala Pro Ser Ser Ser Asp Ser Asp Ser Ser Ser Ser Glu Glu Glu Glu
 35 40 45

Glu Lys Thr Ser Lys Ser Ala Val Lys Lys Lys Pro Gln Lys Val Ala
 50 55 60

Gly Gly Ala Ala Pro Ser Lys Pro Ala Ser Ala Lys Lys Gly Lys Ala
 65 70 75 80

Glu Ser Ser Asn Ser Ser Ser Ser Asp Asp Ser Ser Glu Glu Glu Glu
 85 90 95

Glu Lys Leu Lys Gly Lys Gly Ser Pro Arg Pro Gln Ala Pro Lys Ala
 100 105 110

Asn Gly Thr Ser Ala Leu Thr Ala Gln Asn Gly Lys Ala Ala Lys Asn
 115 120 125

Ser Glu Glu Glu Glu Glu Glu Lys Lys Lys Ala Ala Val Val Val Ser
 130 135 140

Lys Ser Gly Ser Leu Lys Lys Arg Lys Gln Asn Glu Ala Ala Lys Glu
 145 150 155 160

Ala Glu Thr Pro Gln Ala Lys Lys Ile Lys Leu Gln Thr Pro Asn Thr
 165 170 175

Phe Pro Lys Arg Lys Lys Gly Glu Lys Arg Ala Ser Ser Pro Phe Arg
 180 185 190

Arg Val Arg Glu Glu Glu Ile Glu Val Asp Ser Arg Val Ala Asp Asn
 195 200 205

Ser Phe Asp Ala Lys Arg Gly Ala Ala Gly Asp Trp Gly Glu Arg Ala
 210 215 220

Asn Gln Val Leu Lys Phe Thr Lys Gly Lys Ser Phe Arg His Glu Lys
225 230 235 240

Thr Lys Lys Lys Arg Gly Ser Tyr Arg Gly Gly Ser Ile Ser Val Gln
245 250 255

Val Asn Ser Ile Lys Phe Asp Ser Glu
260 265

<210> 225
<211> 1276
<212> PRT
<213> Homo sapien

<400> 225

Met Ile Leu Val Gln Ile Leu Lys Gln Glu Trp Pro Lys His Trp Pro
1 5 10 15

Thr Phe Ile Ser Asp Ile Val Gly Ala Ser Arg Thr Ser Glu Ser Leu
20 25 30

Cys Gln Asn Asn Met Val Ile Leu Lys Leu Leu Ser Glu Glu Val Phe
35 40 45

Asp Phe Ser Ser Gly Gln Ile Thr Gln Val Lys Ser Lys His Leu Lys
50 55 60

Asp Ser Met Cys Asn Glu Phe Ser Gln Ile Phe Gln Leu Cys Gln Phe
65 70 75 80

Val Met Glu Asn Ser Gln Asn Ala Pro Leu Val His Ala Thr Leu Glu
85 90 95

Thr Leu Leu Arg Phe Leu Asn Trp Ile Pro Leu Gly Tyr Ile Phe Glu
100 105 110

Thr Lys Leu Ile Ser Thr Leu Ile Tyr Lys Phe Leu Asn Val Pro Met
115 120 125

Phe Arg Asn Val Ser Leu Lys Cys Leu Thr Glu Ile Ala Gly Val Ser
130 135 140

Val Ser Gln Tyr Glu Glu Gln Phe Val Thr Leu Phe Thr Leu Thr Met
145 150 155 160

348/383

Met Gln Leu Lys Gln Met Leu Pro Leu Asn Thr Asn Ile Arg Leu Ala
 165 170 175

Tyr Ser Asn Gly Lys Asp Asp Glu Gln Asn Phe Ile Gln Asn Leu Ser
 180 185 190

Leu Phe Leu Cys Thr Phe Leu Lys Glu His Asp Gln Leu Ile Glu Lys
 195 200 205

Arg Leu Asn Leu Arg Glu Thr Leu Met Glu Ala Leu His Tyr Met Leu
 210 215 220

Leu Val Ser Glu Val Glu Glu Thr Glu Ile Phe Lys Ile Cys Leu Glu
 225 230 235 240

Tyr Trp Asn His Leu Ala Ala Glu Leu Tyr Arg Glu Ser Pro Phe Ser
 245 250 255

Thr Ser Ala Ser Pro Leu Leu Ser Gly Ser Gln His Phe Asp Val Pro
 260 265 270

Pro Arg Arg Gln Leu Tyr Leu Pro Met Leu Phe Lys Val Thr Glu Arg
 275 280 285

Leu Val Glu Cys Ser Ser Cys Cys Ile Leu Trp Phe Leu Arg Ser Glu
 290 295 300

Ser Lys Tyr Phe Tyr Ile Cys Val Asn Lys Leu Ala Ile Lys Arg Glu
 305 310 315 320

Pro Asn Asn Phe Ser Met Ser Val Glu Asn Gln Asn Met Lys Gly Val
 325 330 335

Glu Ser Arg Thr Leu Ile Leu Lys Ser Val Val Leu Leu Ser Val Ser
 340 345 350

Thr Leu Val Val Ile Ser Leu Gly Lys Phe Ile Ala Thr Cys Gln Ser
 355 360 365

Thr Lys Pro Glu Ser Arg Asn Glu Thr Gln Glu Thr Pro Val Thr Glu
 370 375 380

Val Gly Glu Lys Asn His Ile Lys Thr His Leu Asn Asn Tyr Lys Ala
 385 390 395 400

Ile Phe Val Glu Leu Gln Trp Lys Lys Asn Phe Phe Phe Trp Arg Gln

	405		410		415
Gly Leu Ala	Leu Trp Leu Arg Leu Glu Cys Ser Gly Val Val Ile Ala				
	420		425		430
His Tyr Asn	Leu Glu Leu Leu Asp Tyr Lys Gln Phe Ser Cys Val Ser				
	435		440		445
Leu Pro Ser	Asn Trp Leu Gln Ala His Thr Thr Met Pro Glu Gln Ile				
	450		455		460
Leu Asn Phe	Leu Val Leu Leu His Leu Tyr Leu His Ser Phe Phe Cys				
	465		470		475
					480
Cys Ala Leu	Ser Pro Ser Ile Phe Ile Val Leu Glu Ile Gly Cys His				
			485		490
					495
Phe Val Leu	Leu Lys Leu Leu Ser Asn Ser Trp Pro Gln Gln Phe Phe				
			500		505
					510
Leu Pro Arg	Pro Ser Gly Ile Val Gly Ile Ile Gly Met Asn Pro Tyr				
			515		520
					525
Thr Trp Leu	Ala Cys Gly Phe Phe Gly Phe Val Cys Phe Glu Leu Ser				
			530		535
					540
Phe Tyr Thr	Asn Asp Phe Ser Asp Leu Thr Ile Phe Phe Leu Ile Asp				
			545		550
					555
					560
Ile Leu Leu	Ser Met Val Arg Leu Leu Met Val Ser Arg Met Ala Lys				
			565		570
					575
Pro Glu Glu	Val Leu Val Val Glu Asn Asp Gln Gly Glu Val Val Arg				
			580		585
					590
Glu Phe Met	Lys Asp Thr Asp Ser Ile Asn Leu Tyr Lys Asn Met Arg				
			595		600
					605
Glu Thr Leu	Gly Lys Leu Ile Asn Thr Val Asn Leu Tyr Leu Tyr Lys				
			610		615
					620
Ser Ile Leu	Gly Trp Lys Tyr Ile Leu Gly Asn Val Leu Val Val Ser				
			625		630
					635
					640
Lys Tyr Phe	Leu Asn Val Leu Leu Leu Ile Asn Lys Ile Leu Leu Ile				
			645		650
					655

Ile Ala Phe Glu Thr Met Phe Phe Phe Val Val Tyr Leu Thr His Leu
660 665 670

Asp Tyr Val Asp Thr Glu Arg Ile Met Thr Glu Lys Leu His Asn Gln
675 680 685

Val Asn Gly Thr Glu Trp Ser Trp Lys Asn Leu Asn Thr Leu Cys Trp
690 695 700

Ala Ile Gly Ser Ile Ser Gly Ala Met His Glu Glu Asp Glu Lys Arg
705 710 715 720

Phe Leu Val Thr Val Ile Lys Asp Leu Leu Gly Leu Cys Glu Gln Lys
725 730 735

Arg Gly Lys Asp Asn Lys Ala Ile Ile Ala Ser Asn Ile Met Tyr Ile
740 745 750

Val Gly Gln Tyr Pro Arg Phe Leu Arg Ala His Trp Lys Phe Leu Lys
755 760 765

Thr Val Val Asn Lys Leu Phe Glu Phe Met His Glu Thr His Asp Gly
770 775 780

Val Gln Asp Met Ala Cys Asp Thr Phe Ile Lys Ile Ala Gln Lys Cys
785 790 795 800

Arg Arg His Phe Val Gln Val Gln Val Gly Glu Val Met Pro Phe Ile
805 810 815

Asp Glu Ile Leu Asn Asn Ile Asn Thr Ile Ile Cys Asp Leu Gln Pro
820 825 830

Gln Gln Val His Thr Phe Tyr Glu Ala Val Gly Tyr Met Ile Gly Ala
835 840 845

Gln Thr Asp Gln Thr Val Gln Glu His Leu Ile Glu Lys Tyr Met Leu
850 855 860

Leu Pro Asn Gln Val Trp Asp Ser Ile Ile Gln Gln Ala Thr Lys Asn
865 870 875 880

Val Asp Ile Leu Lys Asp Pro Glu Thr Val Lys Gln Leu Gly Ser Ile
885 890 895

Leu Lys Thr Asn Val Arg Ala Cys Lys Ala Val Gly His Pro Phe Val
900 905 910

Ile Gln Leu Gly Arg Ile Tyr Leu Asp Met Leu Asn Val Tyr Lys Cys
915 920 925

Leu Ser Glu Asn Ile Ser Ala Ala Ile Gln Ala Asn Gly Glu Met Val
930 935 940

Thr Lys Gln Pro Leu Ile Arg Ser Met Arg Thr Val Lys Arg Glu Thr
945 950 955 960

Leu Lys Leu Ile Ser Gly Trp Val Ser Arg Ser Asn Asp Pro Gln Met
965 970 975

Val Ala Glu Asn Phe Val Pro Pro Leu Leu Asp Ala Val Leu Ile Asp
980 985 990

Tyr Gln Arg Asn Val Pro Ala Ala Arg Glu Pro Glu Val Leu Ser Thr
995 1000 1005

Met Ala Ile Ile Val Asn Lys Leu Gly Gly His Ile Thr Ala Glu
1010 1015 1020

Ile Pro Gln Ile Phe Asp Ala Val Phe Glu Cys Thr Leu Asn Met
1025 1030 1035

Ile Asn Lys Asp Phe Glu Glu Tyr Pro Glu His Arg Thr Asn Phe
1040 1045 1050

Phe Leu Leu Leu Gln Ala Val Asn Ser His Cys Phe Pro Ala Phe
1055 1060 1065

Leu Ala Ile Pro Pro Thr Gln Phe Lys Leu Val Leu Asp Ser Ile
1070 1075 1080

Ile Trp Ala Phe Lys His Thr Met Arg Asn Val Ala Asp Thr Gly
1085 1090 1095

Leu Gln Ile Leu Phe Thr Leu Leu Gln Asn Val Ala Gln Glu Glu
1100 1105 1110

Ala Ala Ala Gln Ser Phe Tyr Gln Thr Tyr Phe Cys Asp Ile Leu
1115 1120 1125

352/383

Gln His Ile Phe Ser Val Val Thr Asp Thr Ser His Thr Ala Gly
 1130 1135 1140

Leu Thr Met His Ala Ser Ile Leu Ala Tyr Met Phe Asn Leu Val
 1145 1150 1155

Glu Glu Gly Lys Ile Ser Thr Ser Leu Asn Pro Gly Asn Pro Val
 1160 1165 1170

Asn Asn Gln Ile Phe Leu Gln Glu Tyr Val Ala Asn Leu Leu Lys
 1175 1180 1185

Ser Ala Phe Pro His Leu Gln Asp Ala Gln Val Lys Leu Phe Val
 1190 1195 1200

Thr Gly Leu Phe Ser Leu Asn Gln Asp Ile Pro Ala Phe Lys Glu
 1205 1210 1215

His Leu Arg Asp Phe Leu Val Gln Ile Lys Glu Phe Ala Gly Glu
 1220 1225 1230

Asp Thr Ser Asp Leu Phe Leu Glu Glu Arg Glu Ile Ala Leu Arg
 1235 1240 1245

Gln Ala Asp Glu Glu Lys His Lys Arg Gln Met Ser Val Pro Gly
 1250 1255 1260

Ile Phe Asn Pro His Glu Ile Pro Glu Glu Met Cys Asp
 1265 1270 1275

<210> 226

<211> 632

<212> PRT

<213> Homo sapien

<400> 226

Met Tyr Cys Tyr Ser Ser Ile Lys Phe Cys Ser Leu Phe Ala Phe Glu
 1 5 10 15

Thr Met Phe Phe Phe Val Val Tyr Leu Thr His Leu Asp Tyr Val Asp
 20 25 30

Thr Glu Arg Ile Met Thr Glu Lys Leu His Asn Gln Val Asn Gly Thr
 35 40 45

Glu Trp Ser Trp Lys Asn Leu Asn Thr Leu Cys Trp Ala Ile Gly Ser
 50 55 60

Ile Ser Gly Ala Met His Glu Glu Asp Glu Lys Arg Phe Leu Val Thr
 65 70 75 80

Val Ile Lys Asp Leu Leu Gly Leu Cys Glu Gln Lys Arg Gly Lys Asp
 85 90 95

Asn Lys Ala Ile Ile Ala Ser Asn Ile Met Tyr Ile Val Gly Gln Tyr
 100 105 110

Pro Arg Phe Leu Arg Ala His Trp Lys Phe Leu Lys Thr Val Val Asn
 115 120 125

Lys Leu Phe Glu Phe Met His Glu Thr His Asp Gly Val Gln Asp Met
 130 135 140

Ala Cys Asp Thr Phe Ile Lys Ile Ala Gln Lys Cys Arg Arg His Phe
 145 150 155 160

Val Gln Val Gln Val Gly Glu Val Met Pro Phe Ile Asp Glu Ile Leu
 165 170 175

Asn Asn Ile Asn Thr Ile Ile Cys Asp Leu Gln Pro Gln Gln Val His
 180 185 190

Thr Phe Tyr Glu Ala Val Gly Tyr Met Ile Gly Ala Gln Thr Asp Gln
 195 200 205

Thr Val Gln Glu His Leu Ile Glu Lys Tyr Met Leu Leu Pro Asn Gln
 210 215 220

Val Trp Asp Ser Ile Ile Gln Gln Ala Thr Lys Asn Val Asp Ile Leu
 225 230 235 240

Lys Asp Pro Glu Thr Val Lys Gln Leu Gly Ser Ile Leu Lys Thr Asn
 245 250 255

Val Arg Ala Cys Lys Ala Val Gly His Pro Phe Val Ile Gln Leu Gly
 260 265 270

Arg Ile Tyr Leu Asp Met Leu Asn Val Tyr Lys Cys Leu Ser Glu Asn
 275 280 285

Ile Ser Ala Ala Ile Gln Ala Asn Gly Glu Met Val Thr Lys Gln Pro
 290 295 300

354/383

Leu Ile Arg Ser Met Arg Thr Val Lys Arg Glu Thr Leu Lys Leu Ile
 305 310 315 320

Ser Gly Trp Val Ser Arg Ser Asn Asp Pro Gln Met Val Ala Glu Asn
 325 330 335

Phe Val Pro Pro Leu Leu Asp Ala Val Leu Ile Asp Tyr Gln Arg Asn
 340 345 350

Val Pro Ala Ala Arg Glu Pro Glu Val Leu Ser Thr Met Ala Ile Ile
 355 360 365

Val Asn Lys Leu Gly Gly His Ile Thr Ala Glu Ile Pro Gln Ile Phe
 370 375 380

Asp Ala Val Phe Glu Cys Thr Leu Asn Met Ile Asn Lys Asp Phe Glu
 385 390 395 400

Glu Tyr Pro Glu His Arg Thr Asn Phe Phe Leu Leu Leu Gln Ala Val
 405 410 415

Asn Ser His Cys Phe Pro Ala Phe Leu Ala Ile Pro Pro Thr Gln Phe
 420 425 430

Lys Leu Val Leu Asp Ser Ile Ile Trp Ala Phe Lys His Thr Met Arg
 435 440 445

Asn Val Ala Asp Thr Gly Leu Gln Ile Leu Phe Thr Leu Leu Gln Asn
 450 455 460

Val Ala Gln Glu Glu Ala Ala Ala Gln Ser Phe Tyr Gln Thr Tyr Phe
 465 470 475 480

Cys Asp Ile Leu Gln His Ile Phe Ser Val Val Thr Asp Thr Ser His
 485 490 495

Thr Ala Gly Leu Thr Met His Ala Ser Ile Leu Ala Tyr Met Phe Asn
 500 505 510

Leu Val Glu Glu Gly Lys Ile Ser Thr Ser Leu Asn Pro Gly Asn Pro
 515 520 525

Val Asn Asn Gln Ile Phe Leu Gln Glu Tyr Val Ala Asn Leu Leu Lys
 530 535 540

Ser Ala Phe Pro His Leu Gln Asp Ala Gln Val Lys Leu Phe Val Thr
545 550 555 560

Gly Leu Phe Ser Leu Asn Gln Asp Ile Pro Ala Phe Lys Glu His Leu
565 570 575

Arg Asp Phe Leu Val Gln Ile Lys Glu Phe Ala Gly Glu Asp Thr Ser
580 585 590

Asp Leu Phe Leu Glu Glu Arg Glu Ile Ala Leu Arg Gln Ala Asp Glu
595 600 605

Glu Lys His Lys Arg Gln Met Ser Val Pro Gly Ile Phe Asn Pro His
610 615 620

Glu Ile Pro Glu Glu Met Cys Asp
625 630

<210> 227
<211> 159
<212> PRT
<213> Homo sapien

<400> 227

Met Glu Leu His Tyr Leu Thr His Phe Gln Ile Pro Asp Arg Ile Ser
1 5 10 15

Thr Val Arg Arg Phe Thr Leu Leu Leu Ser Phe Leu Leu Arg Arg Leu
20 25 30

Val Thr Leu Ile Ser Gln Gln Ala Thr Leu Leu Ala Ser Asn Glu Ala
35 40 45

Phe Lys Lys Gln Ala Glu Ser Ala Ser Glu Ala Ala Lys Lys Tyr Met
50 55 60

Glu Glu Asn Asp Gln Leu Lys Lys Gly Ala Ala Val Asp Gly Gly Lys
65 70 75 80

Leu Asp Val Gly Asn Ala Glu Val Lys Leu Glu Glu Glu Asn Arg Ser
85 90 95

Leu Lys Ala Asp Leu Gln Lys Leu Lys Asp Glu Leu Ala Ser Thr Lys
100 105 110

Gln Lys Leu Glu Lys Ala Glu Asn Gln Val Leu Ala Met Arg Lys Gln
115 120 125

Ser Glu Gly Leu Thr Lys Glu Tyr Asp Arg Leu Leu Glu Glu His Ala
 130 135 140

Lys Leu Gln Ala Ala Val Asp Gly Pro Met Asp Lys Lys Glu Glu
 145 150 155

<210> 228
 <211> 313
 <212> PRT
 <213> Homo sapien

<400> 228

Met Gly Ala Glu Ala Ser Ser Ser Trp Cys Pro Gly Thr Ala Leu Pro
 1 5 10 15

Glu Glu Arg Leu Ser Val Lys Arg Ala Ser Glu Ile Ser Gly Phe Leu
 20 25 30

Gly Gln Gly Ser Ser Gly Glu Ala Ala Leu Asp Val Leu Thr His Val
 35 40 45

Leu Glu Gly Ala Gly Asn Lys Leu Thr Ser Ser Cys Gly Lys Pro Ser
 50 55 60

Ser Asn Arg Met Ser Leu Gln Trp Thr Ala Val Ala Thr Phe Leu Tyr
 65 70 75 80

Ala Glu Val Phe Val Val Leu Leu Leu Cys Ile Pro Phe Ile Ser Pro
 85 90 95

Lys Arg Trp Gln Lys Ile Phe Lys Ser Arg Leu Val Glu Leu Leu Val
 100 105 110

Ser Tyr Gly Asn Thr Phe Phe Val Val Leu Ile Val Ile Leu Val Leu
 115 120 125

Leu Val Ile Asp Ala Val Arg Glu Ile Arg Lys Tyr Asp Asp Val Thr
 130 135 140

Glu Lys Val Asn Leu Gln Asn Asn Pro Gly Ala Met Glu His Phe His
 145 150 155 160

Met Lys Leu Phe Arg Ala Gln Arg Asn Leu Tyr Ile Ala Gly Phe Ser
 165 170 175

Leu Leu Leu Ser Phe Leu Leu Arg Arg Leu Val Thr Leu Ile Ser Gln
 180 185 190

Gln Ala Thr Leu Leu Ala Ser Asn Glu Ala Phe Lys Lys Gln Ala Glu
 195 200 205

Ser Ala Ser Glu Ala Ala Lys Lys Tyr Met Glu Glu Asn Asp Gln Leu
 210 215 220

Lys Lys Gly Ala Ala Val Asp Gly Gly Lys Leu Asp Val Gly Asn Ala
 225 230 235 240

Glu Val Lys Leu Glu Glu Glu Asn Arg Ser Leu Lys Ala Asp Leu Gln
 245 250 255

Lys Leu Lys Asp Glu Leu Ala Ser Thr Lys Gln Lys Leu Glu Lys Ala
 260 265 270

Glu Asn Gln Val Leu Ala Met Arg Lys Gln Ser Glu Gly Leu Thr Lys
 275 280 285

Glu Tyr Asp Arg Leu Leu Glu Glu His Ala Lys Leu Gln Ala Ala Val
 290 295 300

Asp Gly Pro Met Asp Lys Lys Glu Glu
 305 310

<210> 229
 <211> 301
 <212> PRT
 <213> Homo sapien

<400> 229

Met Ser Leu Gln Trp Thr Ala Val Ala Thr Phe Leu Tyr Ala Glu Val
 1 5 10 15

Phe Val Val Leu Leu Leu Cys Ile Pro Phe Ile Ser Pro Lys Arg Trp
 20 25 30

Gln Lys Ile Phe Lys Ser Arg Leu Val Glu Leu Leu Val Ser Tyr Gly
 35 40 45

Asn Thr Phe Phe Val Val Leu Ile Val Ile Leu Val Leu Leu Val Ile
 50 55 60

Asp Ala Val Arg Glu Ile Arg Lys Tyr Asp Asp Val Thr Glu Lys Val
 65 70 75 80

Asn Leu Gln Asn Asn Pro Gly Ala Met Glu His Phe His Met Lys Leu
85 90 95

Phe Arg Ala Gln Arg Asn Leu Tyr Ile Ala Gly Phe Ser Leu Leu Leu
100 105 110

Ser Phe Leu Leu Arg Arg Leu Val Thr Leu Ile Ser Gln Gln Ala Thr
115 120 125

Leu Leu Ala Ser Asn Glu Ala Phe Lys Lys Gln Ala Glu Ser Ala Ser
130 135 140

Glu Ala Ala Lys Lys Tyr Met Glu Glu Asn Asp Gln Leu Lys Lys Gly
145 150 155 160

Ala Ala Val Asp Gly Gly Lys Leu Asp Val Gly Asn Ala Glu Val Lys
165 170 175

Leu Glu Glu Glu Asn Arg Ser Leu Lys Ala Asp Leu Gln Lys Leu Lys
180 185 190

Asp Glu Leu Ala Ser Thr Lys Gln Lys Leu Glu Lys Ala Glu Asn Gln
195 200 205

Val Leu Ala Met Arg Lys Gln Ser Glu Gly Leu Thr Lys Glu Tyr Asp
210 215 220

Arg Leu Leu Glu Glu His Ala Lys Leu Gln Ser Pro Ala Ser Pro Ser
225 230 235 240

Ser Thr Ser Val Cys Ala Leu Leu Leu Pro Pro Phe Pro Ser Thr Ala
245 250 255

His Ser Ser Ser Ser Arg Pro Leu Ser Thr Leu Ser Lys His Ile Thr
260 265 270

Gly Asp Leu Ile Ala Thr Arg Ser Glu Cys Val Cys Cys His Pro Ala
275 280 285

Trp Pro Gly Gln Ala Trp His Ser Leu Gly Phe His Ala
290 295 300

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<211> 98

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<223> X=any amino acid

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<222> (73)..(73)

<223> X=any amino acid

<400> 230

Ile Xaa Ser Pro Phe Ser Tyr Thr Pro Pro Phe Pro Pro Thr Gly Gly
1 5 10 15

Ala Ala Leu Ser Ala Arg Gly Ile Xaa Gly Pro Glu Xaa Glu Pro Ala
20 25 30

Ala Ala Ala Val Ala Arg Gly Lys Arg Glu Glu Ala Ala Thr Gly Glu
35 40 45

Lys Lys Arg Ser Arg His Arg Arg Glu Val Asp Thr Gln Ala Ala Ala
50 55 60

Ala Ala Arg Xaa Ala Arg Pro Pro Xaa Arg Pro Ser Pro Arg Pro Val
65 70 75 80

His Lys Ala Ala Arg Leu Arg Lys Gly Val Arg Thr Lys Gly Gln Ser
85 90 95

Leu Gln

<210> 231
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 <223> X=any amino acid

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 <223> X=any amino acid

<400> 231

Phe Xaa Pro Xaa Phe Pro Thr Pro Pro Pro Ser Pro Arg Pro Glu Glu
 1 5 10 15

Pro Leu Phe Pro Arg Gly Ala Phe Xaa Gly Pro Arg Xaa Ser Pro Pro
 20 25 30

Pro Pro Pro Ser Pro Glu Gly Ser Glu Lys Arg Pro Arg Pro Glu Arg
 35 40 45

Lys Ser Gly Val Ala Thr Gly Glu Lys Ser Thr Pro Lys Gln Gln Pro
50 55 60

Pro Pro Xaa Arg Pro Ala His Gln Xaa Ala Arg Pro Pro Ala Pro Ser
65 70 75 80

Thr Lys Gln Pro Ala Ser Ala Lys Gly Tyr Glu Arg Arg Asp Lys Val
85 90 95

Ser Asn Glu Lys Ser Val Glu Asp Arg Lys Glu Val Lys Glu Lys Lys
100 105 110

Glu Lys Thr Lys Gln Thr Ile Ser Cys Pro Gly Gly Ser Glu Lys Xaa
115 120 125

Lys His
130

<210> 232
<211> 260
<212> PRT
<213> Homo sapien

<400> 232

Met Asp Met Ser Leu Glu Leu Asp Ile Ile Lys Leu Asn Arg Ser Gln
1 5 10 15

Arg Gly Gly Trp Gly Gly Cys Arg Gly Leu Arg Ala Val Cys Arg Leu
20 25 30

Pro Val Ala Gly Arg Val Trp Trp Val Leu Gln Ala Ala Ala Gln Val
35 40 45

Asn Arg Gly Gly Gly Pro Ile Arg Asn Arg Pro Gly Ile Ala Leu Arg
50 55 60

Ala Ala Val Glu Gly Gly Arg Asn Arg Pro Ala Pro Tyr Ser Arg Pro
65 70 75 80

Lys Gln Leu Pro Asp Lys Trp Gln His Asp Leu Phe Asp Ser Gly Phe
85 90 95

Gly Gly Gly Ala Gly Val Glu Thr Gly Gly Lys Leu Cys Val Val Ser
100 105 110

Asn Leu Asp Ile Gly Val Ser Asp Ala Asp Ile Gln Glu Leu Phe Ala

362/383

115 120 125

Glu Phe Gly Thr Leu Lys Lys Ala Ala Val His Tyr Asp Arg Ser Gly
130 135 140

Arg Ser Leu Gly Thr Ala Asp Val His Phe Glu Arg Lys Ala Asp Ala
145 150 155 160

Leu Lys Ala Met Lys Gln Tyr Asn Gly Val Pro Leu Asp Gly Arg Pro
165 170 175

Met Asn Ile Gln Leu Val Thr Ser Gln Ile Asp Ala Gln Arg Arg Pro
180 185 190

Ala Gln Ser Val Asn Arg Gly Gly Met Thr Arg Asn Arg Gly Ala Gly
195 200 205

Gly Met Gly Glu Leu Val Glu Ala Pro Arg Arg Arg His Cys Ser Asp
210 215 220

Gly Phe Cys Gly Arg Gly Arg Gly Ala Gly Arg Asn Ser Lys Gln Gln
225 230 235 240

Leu Ser Ala Glu Glu Leu Asp Ala Gln Leu Asp Ala Tyr Asn Ala Arg
245 250 255

Met Asp Thr Ser
260

<210> 233
<211> 243
<212> PRT
<213> Homo sapien

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 <223> X=any amino acid

<400> 233

Thr Glu Pro Glu Pro Ala Arg Arg Leu Gly Arg Val Pro Gly Pro Ala
 1 5 10 15

Cys Arg Val Pro Ala Pro Ser Cys Gly Pro Arg Xaa Trp Gly Ala Ala
 20 25 30

Ala Xaa Val Asn Arg Gly Gly Gly Pro Ser Gly Thr Gly Arg Xaa Ser
 35 40 45

Pro Ala Ala Pro Gly Xaa Arg Gln Glu Pro Thr Gly Ala Leu Gln Gln
 50 55 60

Ala Lys Thr Thr Ser Arg Gln Val Ala Ala Arg Ser Phe Arg Gln Trp
 65 70 75 80

Leu Arg Arg Trp Cys Arg Arg Gly Asp Arg Trp Glu Thr Val Arg Gly
 85 90 95

Val His Leu Asp Xaa Gly Val Ser Asp Ala Asp Ile Gln Glu Leu Phe
 100 105 110

Ala Glu Phe Gly Thr Leu Lys Lys Ala Ala Val His Tyr Asp Arg Ser
 115 120 125

Gly Arg Ser Leu Gly Thr Ala Asp Val His Phe Glu Arg Lys Ala Asp
 130 135 140

Ala Leu Lys Ala Met Lys Gln Tyr Asn Gly Val Pro Leu Asp Gly Arg
 145 150 155 160

Pro Met Asn Ile Gln Leu Val Thr Ser Gln Ile Asp Ala Gln Arg Arg
 165 170 175

Pro Ala Gln Ser Val Asn Arg Gly Gly Met Thr Arg Asn Arg Gly Ala
 180 185 190

Gly Gly Ile Gly Gly Asp Gly Gly Thr Arg Arg Gly Asn Ala Arg Ile
 195 200 205

Leu Cys Gly Arg Gly Arg Gly Ala Gly Arg Asn Ser Lys Gln Gln Leu
 210 215 220

Ser Ala Glu Glu Leu Asp Ala Gln Leu Asp Ala Tyr Asn Ala Arg Met
 225 230 235 240

Asp Thr Ser

<210> 234
 <211> 428
 <212> PRT
 <213> Homo sapien

<400> 234

Met Thr Val Ala Glu Ile Lys Gly Thr Thr Gly Arg Thr Tyr Val Gly
 1 5 10 15

Ser His Ala Gln Gly Arg Ser Ser Lys Cys Leu Lys Lys Thr Lys Thr
 20 25 30

Glu Asn Pro Thr Asp Pro His Gln Thr Arg Trp Thr Arg Ser Gly Gln
 35 40 45

Arg Leu His Arg Gly Thr Gln Ser Val Arg Gln His Ala Trp Ser Met
 50 55 60

His Gly Pro Lys Ser Lys Asn Ala Lys His Ser Met Asp Gln His Thr
 65 70 75 80

His Gly Gln Cys His Val Asp Ile Val Thr Arg Cys Met Phe Ile Cys
 85 90 95

Thr Gly Gln Thr Val Thr Gly His His Pro Thr Ser Thr Ala Ala Glu
 100 105 110

Thr Ser Met Glu Met Ile Asn Ser Val Arg Ala Thr Val Ala Gln Arg
 115 120 125

Glu Ser Met Cys His Leu Arg Glu Ala Ala Tyr Thr Val Val Pro Thr
 130 135 140

Gly Ile Ala His His Val Leu Ala Leu Asp Glu Ser Lys Ala Lys Leu
 145 150 155 160

Ser Ser Asp Val Leu Thr Leu Leu Ile Lys Gln Tyr Cys Arg Glu Ser
 165 170 175

Gly Val Arg Asn Leu Gln Lys Gln Val Glu Lys Val Leu Arg Lys Ser
 180 185 190

Ala Tyr Lys Ile Val Ser Gly Glu Ala Glu Ser Val Glu Val Thr Pro
 195 200 205

Glu Asn Leu Gln Asp Phe Val Gly Lys Pro Val Phe Thr Val Glu Arg
 210 215 220

Met Tyr Asp Val Thr Pro Pro Gly Val Val Met Gly Leu Ala Trp Thr
 225 230 235 240

Ala Met Gly Gly Ser Thr Leu Phe Val Glu Thr Ser Leu Arg Arg Pro
 245 250 255

Gln Asp Lys Asp Ala Lys Gly Asp Lys Asp Gly Ser Leu Glu Val Thr
 260 265 270

Gly Gln Leu Gly Glu Val Met Lys Glu Ser Ala Arg Ile Ala Tyr Thr
 275 280 285

Phe Ala Arg Ala Phe Leu Met Gln His Ala Pro Ala Asn Asp Tyr Leu
 290 295 300

Val Thr Ser His Ile His Leu His Val Pro Glu Gly Ala Thr Pro Lys
 305 310 315 320

Asp Gly Pro Ser Ala Gly Cys Thr Ile Val Thr Ala Leu Leu Ser Leu
 325 330 335

Ala Met Gly Arg Pro Val Arg Gln Asn Leu Ala Met Thr Gly Glu Val
 340 345 350

Ser Leu Thr Gly Lys Ile Leu Pro Val Gly Gly Ile Lys Glu Lys Thr
 355 360 365

Ile Ala Ala Lys Arg Ala Gly Val Thr Cys Ile Val Leu Pro Ala Glu
 370 375 380

Asn Lys Lys Asp Phe Tyr Asp Leu Ala Ala Phe Ile Thr Glu Gly Leu

367/383

145						150						155					160
Asp	Tyr	Leu	Val	Thr	Ser	His	Ile	His	Leu	His	Val	Pro	Glu	Gly	Ala		
				165					170					175			
Thr	Pro	Lys	Asp	Gly	Pro	Ser	Ala	Gly	Cys	Thr	Ile	Val	Thr	Ala	Leu		
			180					185					190				
Leu	Ser	Leu	Ala	Met	Gly	Arg	Pro	Val	Arg	Gln	Asn	Leu	Ala	Met	Thr		
		195					200					205					
Gly	Glu	Val	Ser	Leu	Thr	Gly	Lys	Ile	Leu	Pro	Val	Gly	Gly	Ile	Lys		
	210					215					220						
Glu	Lys	Thr	Ile	Ala	Ala	Lys	Arg	Ala	Gly	Val	Thr	Cys	Ile	Val	Leu		
225					230					235					240		
Pro	Ala	Glu	Asn	Lys	Lys	Asp	Phe	Tyr	Asp	Leu	Ala	Ala	Phe	Ile	Thr		
			245						250					255			
Glu	Gly	Leu	Glu	Val	His	Phe	Val	Glu	His	Tyr	Arg	Glu	Ile	Phe	Asp		
			260					265					270				
Ile	Ala	Phe	Pro	Asp	Glu	Gln	Ala	Glu	Ala	Leu	Ala	Val	Glu	Arg			
		275					280					285					
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<211>	247																
<212>	PRT																
<213>	Homo sapien																
<400>	236																
Met	Ser	Leu	Ala	Ile	Leu	Glu	Glu	Val	Ile	Met	Trp	Asp	Pro	Arg	Val		
1				5					10					15			
Ser	Arg	Pro	Cys	Leu	Pro	Leu	Gly	His	Val	Ala	Thr	Gln	Tyr	Phe	Ala		
			20					25					30				
Glu	Gln	Gly	His	Ala	Ser	Val	Gly	Trp	Ala	Glu	Tyr	Pro	Glu	Glu	Asp		
		35					40					45					
Leu	Lys	Arg	Thr	Met	Met	Ala	Cys	Gly	Gly	Ser	Asn	Pro	Asp	Gln	Cys		
	50					55					60						
Glu	Gly	Ser	Val	Ser	Arg	Leu	Cys	Leu	Ala	Arg	Cys	Gln	Val	Phe	Glu		
65					70					75					80		

Glu Thr Gln Leu Gly Gly Glu Arg Tyr Asn Leu Phe Asp Trp Leu Pro
 85 90 95

Gln Ala Lys Thr Cys Thr Phe Ile Leu Arg Gly Gly Thr Glu Gln Phe
 100 105 110

Met Glu Glu Thr Glu Arg Ser Leu His Asp Ala Ile Met Ile Val Met
 115 120 125

Arg Ala Ile Lys Asn Asp Ser Val Val Ala Gly Gly Gly Ala Ile Glu
 130 135 140

Met Glu Leu Ser Lys Tyr Leu Arg Asp Tyr Ser Arg Thr Ile Pro Gly
 145 150 155 160

Lys Gln Gln Leu Leu Ile Gly Ala Tyr Ala Lys Ala Leu Glu Ile Ile
 165 170 175

Pro Arg Gln Leu Cys Asp Asn Ala Gly Phe Asp Ala Thr Asn Ile Leu
 180 185 190

Asn Lys Leu Arg Ala Arg His Ala Gln Gly Gly Thr Trp Tyr Gly Val
 195 200 205

Asp Ile Asn Asn Glu Asp Ile Ala Asp Asn Phe Glu Ala Phe Val Trp
 210 215 220

Glu Pro Ala Met Val Arg Ile Asn Ala Leu Thr Ala Ala Ser Glu Ala
 225 230 235 240

Ala Val Pro Asp Arg Val Leu
 245

<210> 237
 <211> 154
 <212> PRT
 <213> Homo sapien

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 <223> X=any amino acid

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 <223> X=any amino acid

<400> 237

Leu Leu Pro Gln Ala Lys Thr Cys Thr Phe Ile Leu Arg Gly Gly Thr
 1 5 10 15

Glu Gln Phe Met Glu Glu Thr Glu Arg Ser Leu His Asp Ala Ile Met
 20 25 30

Ile Val Xaa Arg Ala Ile Lys Asn Asp Ser Val Val Ala Gly Gly Gly
 35 40 45

Ala Ile Xaa Met Glu Leu Ser Lys Tyr Leu Arg Asp Tyr Ser Arg Thr
 50 55 60

Ile Pro Gly Lys Gln Gln Leu Leu Ile Gly Ala Tyr Ala Lys Ala Leu
 65 70 75 80

Glu Ile Ile Pro Arg Gln Leu Cys Asp Asn Ala Gly Phe Asp Ala Thr
 85 90 95

Asn Ile Leu Asn Lys Leu Arg Ala Arg His Ala Gln Gly Gly Thr Trp
 100 105 110

Tyr Gly Val Asp Ile Asn Asn Glu Asp Ile Ala Asp Asn Phe Glu Ala
 115 120 125

Phe Val Trp Glu Pro Ala Met Val Arg Ile Asn Ala Leu Thr Ala Ala
 130 135 140

Ser Glu Ala Ala Val Pro Asp Arg Val Leu
 145 150

<210> 238

<211> 269

<212> PRT

<213> Homo sapien

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<223> X=any amino acid

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<223> X=any amino acid

<400> 238

Met Ala Met Asp Leu Cys Arg Gln Asp Pro Glu Cys Glu Phe Tyr Phe
1 5 10 15

Ser Xaa Asp Ala Asp Ala Val Leu Thr Asn Xaa Gln Thr Leu Xaa Xaa
20 25 30

Leu Ile Glu Glu Xaa Arg Gly Val Xaa Ala Pro Met Xaa Xaa Xaa Xaa
35 40 45

Gly Lys Xaa Trp Ser Asn Xaa Trp Gly Xaa Leu Ser Xaa Asp Glu Tyr
50 55 60

Tyr Ala Arg Ser Xaa Asp Xaa Val Glu Leu Val Xaa Arg Lys Asp Val
65 70 75 80

Gly Val Trp Asn Val Pro Tyr Ile Xaa Xaa Ala Tyr Val Xaa Gly Gly
85 90 95

Asp Thr Xaa Xaa Met Glu Leu Pro Gln Arg Asp Val Phe Ser Gly Ser
100 105 110

Asp Xaa Asp Xaa Asp Met Ala Phe Cys Glu Xaa Phe Gly Xaa Lys Gly
115 120 125

Ile Phe Xaa His Leu Ser Tyr Gln His Glu Phe Gly Arg Leu Leu Ala
130 135 140

Thr Ser Arg Tyr Asp Thr Glu His Leu His Pro Asp Leu Trp Gln Ile
145 150 155 160

Phe Asp Asn Pro Val Asp Trp Lys Glu Gln Tyr Ile His Glu Asn Tyr
165 170 175

Ser Arg Ala Leu Glu Gly Lys Asp Ile Val Glu Gln Pro Cys Pro Asp
180 185 190

Val Tyr Trp Phe Pro Leu Leu Ser Glu Gln Met Cys Asp Glu Leu Val
195 200 205

Ala Glu Met Glu His Tyr Gly Gln Trp Ser Gly Gly Arg His Glu Asp
210 215 220

373/383

Ser Arg Leu Ala Gly Gly Tyr Glu Asn Val Pro Thr Val Asp Xaa Pro
 225 230 235 240

His Glu Ala Gly Gly Val Arg Gly Pro Val Ala Ala Ala Ala Asp
 245 250 255

Val Cys Gly Pro Met Thr Xaa Thr Cys Phe Arg Phe Thr
 260 265

<210> 239
 <211> 138
 <212> PRT
 <213> Homo sapien

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 <222> (117)..(117)
 <223> X=any amino acid

<400> 239

Xaa Phe Xaa Xaa Lys Gly Ile Phe Xaa His Leu Ser Tyr Gln His Glu
 1 5 10 15

Phe Gly Arg Leu Leu Ala Thr Ser Arg Tyr Asp Thr Glu His Leu His
 20 25 30

Pro Asp Leu Trp Gln Ile Phe Asp Asn Pro Val Asp Trp Lys Glu Gln
 35 40 45

Tyr Ile His Glu Asn Tyr Ser Arg Ala Leu Glu Gly Lys Glu Ser Trp
 50 55 60

Ser Ser His Ala Arg Thr Cys Thr Gly Ser His Cys Cys Gln Asn Lys
 65 70 75 80

Cys Val Met Ser Trp Trp Gln Arg Trp Ser Thr Thr Ala Ser Gly Gln
85 90 95

Ala Ala Gly Met Arg Ile Gln Gly Trp Leu Glu Ala Thr Arg Met Cys
100 105 110

Pro Pro Trp Thr Xaa His Met Lys Gln Val Gly Tyr Glu Asp Gln Trp
115 120 125

Leu Gln Leu Leu Arg Thr Tyr Val Gly Pro
130 135

<210> 240
<211> 233
<212> PRT
<213> Homo sapien

<400> 240

Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser Asn Ser Cys Cys
1 5 10 15

Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr
20 25 30

Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala
35 40 45

Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe
50 55 60

Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu
65 70 75 80

Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln
85 90 95

Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe
100 105 110

Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile Tyr Pro Asn Ser
115 120 125

Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe Pro Tyr Arg Asp
130 135 140

375/383

Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu Ile Ile Leu Leu
145 150 155 160

Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu Ile Ser Cys Val
165 170 175

Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu
180 185 190

Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Pro Tyr Asp
195 200 205

Asp Ala Thr Val Asn Gly Ala Cys Gln Gly Ala Pro Ala Pro Tyr Val
210 215 220

Leu Pro Lys Pro Ser Ser Gly Arg Thr
225 230

<210> 241

<211> 319

<212> PRT

<213> Homo sapien

<220>

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<222> (2)..(5)

<223> X=any amino acid

<400> 241

Val Xaa Xaa Xaa Xaa Ser Pro Pro Leu Gln Pro Ser Pro Ser Glu Arg
1 5 10 15

Arg Val Pro Thr Arg Gln Lys Leu Gly Ala Leu Gly Val Ser Arg Arg
20 25 30

Gln Ala Arg Gly Arg Thr Gly Glu Arg Ala Gly Ser Arg Ser Gly Gly
35 40 45

Gly Ala Gly Ser Ser Gly Ala Ala Gly Ser Arg Arg Gly Gly Leu Gln
50 55 60

Ala Arg Arg Ser Thr Leu Leu Lys Thr Cys Ala Arg Ala Arg Ala Thr
65 70 75 80

Ala Pro Gly Ala Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser
85 90 95

376/383

Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu
 100 105 110

Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu
 115 120 125

Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu
 130 135 140

Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile
 145 150 155 160

Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly
 165 170 175

Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln
 180 185 190

Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile
 195 200 205

Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe
 210 215 220

Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu
 225 230 235 240

Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu
 245 250 255

Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser
 260 265 270

Ser Asp Val Leu Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu
 275 280 285

Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala Cys Gln Gly Ala Pro
 290 295 300

Ala Leu Thr Cys Cys Leu Ser Leu Gln Val Gly Gly Pro Glu Gly
 305 310 315

<210> 242

<211> 76

<212> PRT

<213> Homo sapien

377/383

<400> 242

Met Asp Ser Ser Gly Ala Arg Ala Gly Thr Val Cys Thr Leu His Gly
1 5 10 15

Ile His Arg Gly His Gln Lys Pro Gly Leu Phe Leu Ser Arg Ser Ser
20 25 30

Asn Val Phe Ser Ser Asp Ser His His Leu Gln Leu Val Pro Thr Gln
35 40 45

Cys Cys His Ser Arg Leu Thr Gln Val Leu Arg Pro Ser Thr Ser Ser
50 55 60

Ala Ala Arg Ala His Leu Arg Leu Asp Cys Thr Ile
65 70 75

<210> 243

<211> 72

<212> PRT

<213> Homo sapien

<400> 243

Arg Ser Gly Cys Leu Ile Tyr Gly Leu Ala Leu Asp Ala Pro Ser Gly
1 5 10 15

Arg Ser Val Met Asp Ser Ser Gly Ala Arg Ala Gly Thr Val Cys Thr
20 25 30

Leu His Gly Ile His Arg Gly His Gln Lys Pro Gly Leu Phe Leu Ser
35 40 45

Arg Ser Ser Asn Ala Ser Ala Ala Ile Ala Thr Thr Tyr Ser Ser Ser
50 55 60

Pro His Ser Ala Ala Thr Ala Gly
65 70

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<212> PRT

<213> Homo sapien

<400> 244

Met Gly Phe Ile Glu Ala Thr Arg Asn Gln Ala Phe Ser Cys Pro Glu
1 5 10 15

Val Pro Ser Phe Ser Ser Asp Ser His His Leu Gln Leu Val Pro Thr

378/383

20

25

30

Gln Cys Cys His Ser Arg Leu Thr Gln Val Leu Arg Pro Ser Thr Ser
35 40 45

Ser Ala Ala Arg Ala His Leu Arg Leu Asp Cys Thr Ile
50 55 60

<210> 245
<211> 57
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Arg Pro Pro Glu Thr Arg Pro Phe Leu Val Gln Lys Phe Gln Arg Phe
1 5 10 15

Ser Ser Asp Ser His His Leu Gln Leu Val Pro Thr Gln Cys Cys His
20 25 30

Ser Arg Leu Thr Gln Val Leu Arg Pro Ser Thr Ser Ser Ala Ala Arg
35 40 45

Ala His Leu Arg Leu Asp Cys Thr Ile
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Ala Asp Glu Thr Ser Glu Lys Glu Gln Gln Glu Ala Ile Glu His Ile
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Asp Glu Val Gln Asn Glu Ile Asp Arg Leu Asn Glu Gln Ala Ser Glu
20 25 30

379/383

Glu Ile Leu Lys Val Glu Gln Lys Tyr Asn Lys Leu Arg Gln Pro Phe
35 40 45

Val Gln Lys Arg Ser Glu Leu Ile Ala Lys Ile Pro Thr Phe Leu Gly
50 55 60

Asn Asn Ile Cys Gln Pro Ser Thr Ser Val Cys Thr Ala Leu Arg Glu
65 70 75 80

Glu Asp Glu Glu Ala Leu His Tyr Leu Thr Arg Val Glu Val Thr Glu
85 90 95

Phe Glu Asp Ile Lys Ser Gly Tyr Arg Ile Asp Phe Asp Phe Asp Gly
100 105 110

Asn Pro Tyr Phe Glu Asn Lys Val Leu Ser Lys Glu Phe His Leu Asn
115 120 125

Glu Ser Gly Asp Pro Ser Ser Lys Ser Thr Glu Ile Lys Trp Lys Ser
130 135 140

Gly Lys Asp Leu Thr Lys Arg Ser Ser Gln Thr Gln Asn Lys Ala Ser
145 150 155 160

Arg Lys Arg Gln His Glu Glu Pro Glu Ser Phe Phe Thr Trp Phe Thr
165 170 175

Asp His Ser Asp Ala Gly Ala Asp Glu Leu Gly Glu Val Ile Lys Asp
180 185 190

Asp Ile Trp Pro Asn Pro Leu Gln Tyr Tyr Leu Val Pro Asp Met Asp
195 200 205

Asp Glu Glu Gly Glu Gly Glu Glu Asp Asp Asp Asp Asp Glu Glu Glu
210 215 220

Glu Gly Leu Glu Asp Ile Ala Lys Asn Gly Asp Glu Asp Glu Gly Asp
225 230 235 240

Gly Met Met Lys Ile Asp Asp Glu Val Gly Gly Thr Glu Gln Gly Gly
245 250 255

Leu Lys Lys Lys Phe Leu Xaa Xaa Pro Pro Xaa
260 265

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<400> 247

Ser Phe Xaa Phe Asp Gly Asn Pro Tyr Phe Glu Asn Lys Val Leu Ser
 1 5 10 15

Xaa Glu Phe His Leu Asn Glu Ser Gly Asp Pro Ser Ser Lys Ser Thr
 20 25 30

Glu Ile Lys Trp Lys Ser Gly Lys Asp Leu Thr Lys Arg Ser Ser Gln
 35 40 45

Thr Gln Asn Lys Ala Ser Arg Lys Arg Gln His Glu Glu Pro Glu Ser
 50 55 60

Phe Phe Thr Trp Phe Thr Asp His Ser Asp Ala Gly Ala Asp Glu Leu
 65 70 75 80

381/383

Gly Glu Val Ile Lys Asp Asp Ile Trp Pro Asn Pro Leu Gln Tyr Tyr
 85 90 95

Leu Val Pro Asp Met Asp Asp Glu Glu Gly Glu Gly Glu Glu Asp Asp
 100 105 110

Asp Asp Asp Glu Glu Glu Glu Gly Leu Glu Asp Ile Ala Lys Lys Gly
 115 120 125

Met Arg Met Lys Val Xaa Lys Xaa Lys Xaa Xaa Met Xaa Trp Glu Glu
 130 135 140

Gly Gln Glu Asp
 145

<210> 248
 <211> 234
 <212> PRT
 <213> Homo sapien

<400> 248

Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser Asn Ser Cys Cys
 1 5 10 15

Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr
 20 25 30

Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala
 35 40 45

Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe
 50 55 60

Glu Phe Met Asp Asp Ala Lys Ile Leu Phe Asn Leu Ser Ala Asp Met
 65 70 75 80

Cys Ile Ala Ile Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met
 85 90 95

Ala Thr Tyr Gly Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe
 100 105 110

Phe Cys Tyr Gln Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile
 115 120 125

Thr Val Leu Ile Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu

130 135 140

Pro Pro Asn Phe Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr
145 150 155 160

Cys Leu Val Leu Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr Phe
165 170 175

Lys Gly Tyr Leu Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile Asn
180 185 190

Gly Arg Asn Ser Ser Asp Val Leu Val Tyr Val Thr Ser Asn Asp Thr
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Thr Val Leu Leu Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala Ala
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Lys Glu Pro Pro Pro Pro Tyr Val Ser Ala
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25

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<400> 250
caggagcatc tccgttttca tt

22

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<212> DNA
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<220>
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<400> 251
tccagtagtt gggcagtgct ggca

24

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<212> DNA
<213> Artificial Sequence

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<400> 252
tcggcagaca tgtgcattg

19

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cgttgcttgt acgctccgta a

21

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<212> DNA
<213> Artificial sequence

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<223> Synthetic

<400> 254
cattgcgatt tctcttctca tgatcctgat atg

33

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